Library

MAR 6 1946

VOLUME 35 (OLD SERIES VOLUME 93) NUMBER 1

ARCHIVES OF

OPHTHALMOLOGY

Continuing the Publication
FOUNDED BY HERMAN KNAPP, 1869

EDITORIAL BOARD

ARNOLD KNAPP, Chief Editor
10 East Fifty-Fourth Street, New York 22

WILLIAM ZENTMAYER, Philadelphia
FREDERICK C. CORDES, San Francisco
W. L. BENEDICT, Rochester, Minn.
FRANCIS HEED ADLER, Philadelphia
DAVID G. COGAN, Boston

JANUARY 1946

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

COPYRIGHT, 1946, BY THE AMERICAN MEDICAL ASSOCIATION

ARCHIVES OF OPHTHALMOLOGY

VOLUME 35 (old series Volume 92) JANUARY 1946 NUMBER 1

COPYRIGHT, 1946, BY THE AMERICAN MEDICAL ASSOCIATION

OCCURRENCE OF GLIOMA OF RETINA AND BRAIN IN COLLATERAL LINES IN SAME FAMILY

GENETICS OF GLIOMA

ANDREW RADOS, M.D.
NEWARK, N. J.

Heredity depends on the intrinsic factors, the genes, and on extrachromosomal influences. Mendelian inheritance is through the chromosomes, and the various traits are carried by the hypothetic biochemical units called genes. The factor of heredity in malignant tumors is of minor importance, with the exception of glioma and neurofibromatosis (von Recklinghausen's disease), in which the hereditary influence is generally recognized and accepted. In addition to these two types of tumors, Lehmann [1] stated that polyposis of the rectum is irregularly dominant, a precancerous condition, with a possibility of development into cancer in 75 per cent of cases, and that xeroderma pigmentosum has a recessive inheritance, with consanguinity in 25 per cent of cases. Xeroderma pigmentosum, with an inborn excess of porphyrins, like polyposis of the rectum, represents a precancerous state, a hereditary hypersensitiveness of the skin to sunlight, especially the ultraviolet rays, resulting in development of carcinoma of the skin, even in childhood. The aforementioned tumors occurring in man have in common that the role of heredity is proved. Among animals, the adenocarcinoma of mice is strikingly hereditary, and in Drosophila two kinds of spontaneous tumors are recognized—melanoma, with a recessive gene in the X chromosome, and a benign growth, with a recessive gene in the third chromosome. In contrast to retinoblastoma, in which, according to Wells,[2] the hereditary factor is conspicuous, are other types of tumors which tend to be congenital or to appear in early infancy without any hereditary factor. Among these are mixed malignant renal neoplasm (Wilms's tumor), neuroblastoma of the adrenal medulla and other parts of the sympathetic nervous system, congenital hepatic hemangioendothelioma, congenital sarcoma, endothelioma, melanoma, tumors of the testis, chordoma and the leukemias.

Weller [3] pointed out that from the standpoint of the study of the intrinsic factors in malignant growths gliomas have a distinct advantage over carcinomas. The hereditary disposition in families with carcinoma is often obscured by death at any time prior to the physiologic limit of life. The evidence for the hereditary factor in gliomas occurring in infancy or in early childhood, on the other hand, is limited only by their occurrence in stillborn children and in children dying in early infancy.

Gliomas are relatively rare. According to Leber [4] the incidence was less than 0.04 per cent in a large statistical series, and according to Hemmes it was 1 in 24,000 living births. A recent review of the entire literature up to 1943 has been made by Benedict and Parkhill.[5] In the majority of the articles in the literature sporadic cases are considered, but even the early observers noted the familial trend. Von Lerche (1821) was the first to report an instance of such a trend, that of a family of 7 children, in which 3 boys and 1 girl had retinal glioma. Leber,[4] in his masterful monograph on retinal diseases, mentioned 15 families with 2 affected children, 6 families with 3 affected children, 4 families with 4 affected children, 1 family with 5 affected children, 1 family with 8 affected children and 1 family with 10 affected children. A review of cases of multiple occurrence shows that Newton reported a family with 10 affected children (3 with unilateral and 7 with bilateral retinal glioma) out of 16; Thompson and Knapp, one with 5 affected children out of 14; Calderini, one with 3 affected children out of 14; Leber,

From the Ophthalmic Department and Laboratory of the Beth-Israel Hospital.

1. Lehmann, W.: Kritische Uebersicht: Krebs und Vererbung, Med. Klin. **38**:567, 1942.

2. Wells, H. G.: Occurrence and Significance of Congenital Malignant Neoplasms, Arch. Path. **30**:535 (Aug.) 1940.

3. Weller, C. V.: The Inheritance of Retinoblastoma and Its Relationship to Practical Eugenics, Cancer Research **1**:517, 1941.

4. Leber, T.: Die Krankheiten der Netzhaut: Das Gliom, in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, W. Engelmann, 1916, vol. 7 A, p. 1723.

5. Benedict, W. L., and Parkhill, E. M.: Glioma of the Retina in Successive Generations, Am. J. Ophth. **26**:511, 1943.

one with 3 affected children out of 9; Maher, one with 3 affected children out of 3; Wilson, one with 8 affected children out of 18; von Lerche, one with 4 affected children out of 7; de Gouvêa, one with 2 affected children out of 7; von Graefe, one with 2 affected children out of 7; Marshall, one with 3 affected out of 6; Macgregor, one with 3 affected children (bilateral glioma) out of 5; Cirincione and Calderaro, each a family with 4 affected children out of 5; Schönemann, a family with 2 affected children out of 3; Valenti, Fuchs, Snell and von Hoffmann, each a family with 2 affected children out of 3; Sichel, a family with 4 affected children out of 4; Snell, 2 affected children; Steinhaus and Owen, each a family with 2 affected children out of 2; Dabney, a family with 3 affected children out of 3 (2 with bilateral and 1 with unilateral glioma); Comas, a family with 5 affected children out of 11, and Weller, a family with 6 affected children out of 10 (2 with bilateral glioma). The familial occurrence was reported by Adam in 3 families, each of them with 2 afflicted children. In this connection, I wish to mention a family of 4 children in which I observed 4 afflicted children (2 with bilateral and 2 with unilateral involvement). One of the most interesting observations is that of Townsend. A Negro woman had a daughter with glioma of the retina. The mother gave birth to 2 daughters by another father; both the children had glioma. The occurrence of families with retinoblastoma, the expression of horizontal inheritance, has been known for many years and points to the hereditary character of glioma; but the majority of cases of this tumor are sporadic, without similar cases either in the ascendants or in the descendants. Hemmes found no familial occurrence in 48 cases; Bucklers, none in 49 cases; Stock, none in 28 cases; Sabugin, none in 14 cases (of sisters and brothers, but not parents), and Davenport, none in 27 cases. Reiser[6] discovered 1 case in 16 families, with a total of 64 children; Griffith and Sorsby,[7] tabulating the glioma material of the Royal Eye Hospital, in London, between 1894 and 1943, discovered 53 isolated cases and 6 cases occurring within 1 family in three successive generations. Leber reported on 25 families with multiple occurrence of glioma, mostly among sisters and brothers, and Bell,[8] on 36 families. Hemmes increased the number (including those reported on by Fietta, van der Hoeve and Mayer-Riemsloh) to 39 families. According to Reiser, there are recorded in the literature about 50 families with multiple occurrence of glioma; this number includes the 467 cases of Wintersteiner. Considering that about 1,000 cases have been reported in the literature, one has to assume that cure through operation has been attained in 40 or 50 per cent, so that a large number of patients with healed glioma reach the reproductive age; this is in apparent contradiction to the known cases of hereditary transmission.

The multiple occurrence of retinal glioma in the same family and, similarly, the transmission of glioma to the offspring in successive generations were known, but only recently has the vertical familial distribution and the collateral mode of inheritance been appreciated. Transmission from generation to generation, the so-called vertical inheritance, is one of the most important factors in the heredity of disease. Von Graefe was the first to report the transmission of glioma through two generations. De Gouvêa enucleated the right eye of a boy at the age of 2 years; he survived and 2 of his 7 children were afflicted with bilateral glioma. According to Owen, in Bowman's case the father's left eye was enucleated at the age of 5 years; his son had glioma at the age of 3 years, and 2 children of the father's sister were similarly affected. In the family reported by von Hoffmann the mother's left eye was enucleated at the age of 2 years, and twenty-eight years later the first son had bilateral glioma; the second son, similarly, had bilateral glioma at the age of 4 months, and the third child is still free of glioma, at the age of 7 months. Steinhaus and Caspar independently described the occurrence of glioma in a mother and daughter. Griffith observed 2 families with glioma. In the first family, the mother had had one eye removed at the age of 9 months, and 4 of her 7 children had bilateral glioma; in the second family, the mother lost one eye, and 3 of her 4 children were afflicted (1 with bilateral and 2 with unilateral glioma). Taylor observed a child with glioma whose mother lost one eye in childhood, presumably of glioma. In the case of de Haas a child with bilateral glioma was the offspring of a father whose right eye was enucleated for the same condition. In Pockley's case both the father's eyes had been lost on account of glioma, and he had a child with bilateral glioma. In the latter case there was not only vertical but horizontal inheritance, as the father was identified with the family reported on by Maher, in which

6. Reiser, K. A.: Bemerkungen zur Erblichkeitsfrage beim Glioma retinae, Klin. Monatsbl. f. Augenh. **99**:350, 1937.

7. Griffith, A. D., and Sorsby, A.: The Genetics of Retinoblastoma, Brit. J. Ophth. **28**:279, 1944.

8. Bell, J.: The Treasury of Human Inheritance, London, Cambridge University Press, 1922, vol. 2, pt. 1.

both sisters had bilateral glioma. In the family reported by Traquair the father's left eye had been enucleated by Argyll Robertson for tumor (apparently glioma) at the age of 6 months; the first child was stillborn, and the second exhibited bilateral, and the third unilateral, glioma. In the family reported by Sym, one of the father's eyes was enucleated by Argyll Robertson for a similar reason; the first child was stillborn; the second and third children died of bilateral glioma at the age of 4 years, and the fourth child, a girl, was still normal, at the age of 3 years. Fietta and Odinzow described a case of transmission from mother to daughter; in the family recorded by van der Hoeve the father had unilateral glioma, and 2 of his 12 children had glioma duplex. In the family reported by Letchworth the father lost one eye, and of his 5 children, 1 was stillborn and 3 had glioma (2 bilateral and 1 unilateral). Mayer-Riemsloh described transmission from father to son; in the family recorded by Best 1 of the parents and 2 of 3 children had the disease (bilateral in both children); in Stallard's case the father had bilateral glioma (one eye was enucleated; in the other eye the tumor underwent spontaneous regression), and he had 2 sons with bilateral glioma; Reiser, in a series of 16 cases of glioma, mentioned 1 in which the mother transmitted glioma to the son. Lange's series of 36 cases included the cases in 2 families with vertical inheritance of glioma. In the first family the father, with glioma in the left eye, had 2 children with bilateral glioma (the case is identical with that presented by Clausen); in Lange's second family the father, who had unilateral glioma, had a child with bilateral glioma. In the family reported by Weller the father lost his eye on account of glioma and had 2 daughters with glioma (1 with bilateral and the other with unilateral involvement). This family is remarkable because the history revealed that the father's father and the great-grandfather had had one eye removed in childhood. Assuming that these eyes were all enucleated for glioma, the tumor occurred in four successive generations of the same family. Benedict and Parkhill reported 4 cases, a case occurring in each of two successive generations of 2 families. In the first family the mother had unilateral glioma and gave birth to a girl with bilateral glioma. In the second family identical twins were involved; 1 of them died of cerebral extension of unilateral glioma (there was no evidence of glioma of the other eye at the time of death), and the second of the pair had involvement of both eyes; this twin had 2 children, 1 of whom had bilateral glioma. Badtke[9] reported 8 cases in which there was no familial heredity and 2 cases in which there was direct inheritance (from the mother to the second son); Fleischer reported the occurrence of glioma in three generations. Griffith and Sorsby extended the observations of Letchworth, Griffith and Hine, respectively, on the occurrence of glioma in two generations, by reporting its appearance in the third generation of the same family. In the first generation, a man had had one eye enucleated, and he had been cured of the glioma in his other eye; of his 5 children, the first, a premature girl, died on the eighth day after birth. The 4 sons all had glioma (3 with bilateral and 1 with unilateral involvement). The oldest brother (who had been cured of bilateral glioma) had 2 daughters: The first died at the age of 5 weeks, of congenital heart disease; the second had both eyes enucleated because of glioma. If one considers the recent reports, the cases of vertical transmission seem to have increased since attention has been directed to it, as Leber, in 1916, could note only 3 instances (de Gouvêa, Owen, von Hoffmann) of direct transmission, or the more exact knowledge of the disease and early enucleation have resulted in the rescue of more children from death due to the glioma; these persons then reach the age of reproduction and beget gliomatous offspring. It is interesting to note that the family trees of patients with glioma are usually free from other hereditary anomalies, with the exception of the family recorded by Badtke, who noted carcinoma, hydrophthalmos, feeblemindedness, insanity, cirrhosis of the liver and myopia in 6 members of the family afflicted with glioma.

In the recorded cases and in cases already enumerated, the vertical transmission through successive generations was effected through parents (male and female) who themselves had the disease. In the older literature the diagnosis was often only clinical; however, in the more recent literature the clinical diagnosis was confirmed by histologic examination. There is evidence of hereditary transmission in families with glioma through parents not manifesting the disease. This group consists of 8 families; in 4 families the male, and in 4 the female, transmitted the glioma to more than one generation, or it was transmitted through collateral lines. The oldest observation has already been mentioned, that by von Graefe, in which several siblings of the mother of another child (with glioma) died in the first year of life of cancer of the eye. Thompson and Knapp and Thompson, respectively,

9. Badtke, G.: Zur Erblichkeitsfrage beim Glioma retinae, Klin. Monatsbl. f. Augenh. **105**:451, 1940.

reported on a family in which parents who were free from glioma had a son and a daughter with glioma and a cousin of the father died of glioma. The history showed, also, that the father's aunt lost 2 children because of glioma. Thompson, following the same family for twenty-four years, reported that of the 14 children 5 (2 boys and 3 girls) died of glioma, and the father's great-aunt was reported to have had 3 children who died of cancer of the eye. Steinhaus reported on a family with 10 children, 3 of whom had unilateral glioma. The firstborn, a son who was free from glioma, had 2 children, a boy and a girl, each of whom had the left eye enucleated for glioma. Lukens reported the case of a child with bilateral glioma whose cousin on the father's side had died previously of the disease, and the uncle and aunt recognized the appearance of the eye as similar to that of their child. Owen's publication shows a family in which the grandfather's left eye was enucleated by Bowman; his son had unilateral glioma, and the normal daughter had 8 children, 4 of whom had glioma (3 with bilateral and 1 with unilateral involvement). Berrisford reported on the same family; Owen's description makes the mother of the 8 children not the daughter but the sister, of the grandfather. Waardenburg cited Hemmes, namely, that 4 of 7 siblings of the father had glioma, and, although he did not himself have the disease, 4 out of his 5 children were afflicted. Purtscher recorded a family of 11 children, of whom 2 boys died of bilateral glioma; a normal sister had a son who died of glioma of the left eye. In addition, another sister, unmarried, had abnormalities of both eyegrounds, more pronounced in the left eye, which was nearly blind. The original diagnosis was choroiditis or neoplasm, but repeated examinations led to the opinion of spontaneous retrogression of glioma, which apparently occurs more frequently than it is given credit for. Sabugin's 14 cases include those of 2 brothers with glioma duplex; the mother's brother also had retinal glioma, of which he died. One of the most interesting cases falling into this group is that of Townsend, mentioned before, in which the mother, who did not manifest the disease, transmitted glioma to 3 daughters through 2 husbands (one by the first and 2 by the second marriage).

The collected data from the literature are cited in order to demonstrate the horizontal, vertical and collateral hereditance of glioma. In order to determine the role of heredity in a disease it is necessary to study all members of a family through several generations with respect to the presence or absence of the disease. The study of the family tree in man is rather limited through such factors as chance matings, the small number of children and the long life span of generations. The determination of the exact part played by heredity in the production of any character becomes one of the most difficult of problems; hence, observations on identical human twins are of paramount importance. Identical twins derive from the same fertilized ovum and necessarily have the same genetic composition; they are either exact duplicates or mirror images of each other. Any disease or anomaly which develops similarly in the two members of the pair is conditioned by the genetic composition of the chromosomes. The research on twins with respect to tumor has revealed information of tremendous importance. McFarland, with Meade,[10] collected from the literature the largest number of neoplasms in identical twins — 40 tumors (benign and malignant) occurring in 20 pairs of monozygotic twins. Their report included the family described by Silcock,[11] which, similarly, was included in the later compilation of Macklin. The data supplied by Silcock do not warrant the inclusion of his case in the group of tumors of the eye in twins; daughter and mother had melanotic sarcoma of the left eye, with an interval of twenty years. The sister of the mother died of multiple tumor at the age of 40 and lost one eye. A twin sister of this patient, and also her father, lost one eye, but "there was great doubt as to whether in the last 3 cases the loss was due to neoplastic growth." Macklin[12] collected from the literature the cases of 53 pairs of monozygotic and 35 pairs of dizygotic twins with tumor and found that tumor affects both members of a pair of identical twins more frequently than it does both members of a pair of fraternal twins; the age of onset of the tumors shows a similar relation. Of the identical twins, both members were affected by the same type of tumor in the same organ at the same age in 64 per cent, whereas in 36 per cent the other of the pair remained unaffected; of the fraternal twins both members of the pair were afflicted in 33 per cent, which is about one-half the value for the identical twins. Of the identical twins, the tumor affected the same organ in 93 per cent; of the fraternal twins, in only 58 per cent, even

10. McFarland, J.: Problem of Cancer in Twins, Bull. Am. Soc. Control Cancer **25**:40, 1943.

11. Silcock, A. A.: Hereditary Sarcoma of Eyeball in Three Generations, Brit. M. J. **1**:1079, 1892.

12. Macklin, M. T.: Symposium of Gynecologic Cancer, West. J. Surg. **50**:439, 1942; An Analysis of Tumors in Monozygous and Dizygous Twins, J. Hered. **31**:277, 1940.

if they belonged to the same sex. Conversely, Charache [13] presented histories of 3 pairs of homologous twins of which 1 member of each pair was affected, 1 member of 2 pairs having Hodgkin's disease and 1 member of the other pair having osteogenic sarcoma. The 3 affected twins died, and the homologous living members of these pairs had been free of any symptoms for four years and two months, five and one-half years and eight years, respectively, since recognition of the disease in the deceased twin. The basis of identity in twins, the single ovum with division into two blastomeres, each receiving an equal share of genetic influences, material and defects, sheds important light on retinal glioma in identical twins. The material necessarily is scant, and it is surprising to find three papers on the subject. Benedict [14] and Benedict and Parkhill [5] observed glioma in identical twin girls at the age of about 4 years; 1 of the pair had bilateral glioma and the other unilateral glioma (the same family was mentioned in the group of vertical inheritance). Duncan and Maynard [15] described neuroepithelioma in identical twin sisters at the age of 7 months. In both twins the tumor showed well formed rosettes and areas of differentiating fibrillar glial tissue; both patients succumbed, but the type of extension of the tumor was different in the 2 patients, the difference probably being influenced by the circumstance that, because of the hydrophthalmos present in the first case, trephination was done, resulting in subsequent spread from the orbital region to the upper superior cervical glands. The member of the pair who was not subjected to operation died of intracranial extension of the tumor. Moore's [16] case was that of a girl aged 2 years with bilateral glioma, whose twin sister was free of the disease. Unfortunately, no mention is made of whether the twins were identical or fraternal, and therefore the case adds nothing of value to clinical research. The occurrence of retinal glioma in identical twins raises the question of glioma located in parts other than the retina in such twins; surprisingly, data are available on the subject. Joughin [17] reported synchronously expanding intracranial neoplasms in identical twin sisters aged 32, both of whom had development of glioma within one and a half years of each other and died; the family history had been negative for tumor for three generations. Leavitt [18] observed identical twin boys; the first child died at the age of 6½ and the second at the age of 8 years. At the time of death of the first twin the second had not shown any symptoms of illness. Autopsy on the first patient revealed a large infiltrating glioma arising from the root of the fourth ventricle; the cellular structure was identical with that of the medulloblastoma described by Bailey and Cushing, with neuroblasts and spongioblasts in small number. No autopsy was performed on the second boy; however, the diagnosis of cerebellar tumor was unquestioned, but the exact location and histopathologic features of the growth remained unconfirmed.

The similarity in type of tumors in homologous organs with about the same age of onset in monozygotic twins emphasizes the importance of the role played by heredity. The number of cases is as yet too small to permit conclusive evidence. All cases of glioma in twins (identical and fraternal) should therefore be published in the future in order that the ratio of concordance to discordance of monozygotic and dizygotic twins may be established. Considering the relatively small number of available instances, the gathering of such material may consume considerable time, but the effort will be rewarded by conclusive evidence. Habs and Dietel,[19] similarly, collected material on uterine carcinoma and found 8 cases in identical twins and no cases in fraternal twins (there were only 2 pairs of fraternal twins in the series); they concluded that hereditary predisposition to carcinoma of the uterus seems to be assured but not proved, and they urged the compilation of larger series of cases and longer periods of observation of the still unaffected member of the pair. Lehmann pointed out that the ratio of concordance to discordance differs in identical and in fraternal twins, the percentage of concordance in identical twins being larger, considering the localization and type of the tumor; on the basis of these figures carcinoma of the stomach in the twin material shows a hereditary disposition, but the same is not true of carcinoma of other organs.

13. Charache, H.: Tumors in One of Homologous Twins; Hodgkin's Disease; Osteogenic Sarcoma, Am. J. Roentgenol. **46**:69, 1941.

14. Benedict, W. L.: Retinoblastoma in Homologous Eyes of Identical Twins, Arch. Ophth. **2**:545 (Nov.) 1929.

15. Duncan, W. J. L., and Maynard, R. B. M.: Bilateral Glioma in Twins, Tr. Ophth. Soc. Australia **1**: 125, 1939.

16. Moore, E.: Clinical and Pathological Report of Bilateral Glioma Retinae, Proc. Roy. Soc. Med. **22**: 951, 1929.

17. Joughin, J. L.: Coincident Tumor of the Brain in Twins, Arch. Neurol. & Psychiat. **19**:948 (May) 1928.

18. Leavitt, F. H.: Cerebellar Tumors Occurring in Identical Twins, Arch. Neurol. & Psychiat. **19**:617 (April) 1928.

19. Habs, H., and Dietel, H.: Zwillingsforschung bei Uterus-Carcinom, Klin. Wchnschr. **20**:8, 1941.

The gliomatous fraternities, the vertical familial distribution appearing in successive generations or in collateral lines and the research on gliomas of the retina and brain in twins are the factual evidence at one's command in the search for hereditary factors. Further evidence in support of the hereditary basis is the possible connection of glioma of the brain in families with glioma of the retina. Regarding this association, evidence is almost completely lacking. Marshall and Leber mentioned that in a family with multiple glioma of the retina an unafflicted child died suddenly with convulsions, and Vetsch reported 2 families with glioma in which one or two unaffected children died of convulsions or cerebral disease of inflammatory nature. One would have to stretch the imagination to arrive at the diagnosis of glioma of the brain from the scanty reports of these cases. The acceptable case seems to be that of Elschnig cited by Leber, that of a 2 year old girl with unilateral glioma whose 13 year old sister ten years later died of infiltrative glioma of the large hemisphere of the brain. The cases to be reported seem to belong in this group of hereditary influences, and the uniqueness of the observation therefore warrants the detailed report of the family history.

Case 1.—D. W., a boy aged 8 months, had his left eye enucleated. The right eye was treated with roentgen radiation and then enucleated three months later.

The blood group was B. A blood count revealed 8,500 leukocytes, with 35 per cent polymorphonuclear leukocytes, 55 per cent lymphocytes, 11 per cent endothelial leukocytes, 8 per cent eosinophils, 1 per cent stab forms and 48 per cent hemoglobin. Erythrocytes numbered 3,350,00 with marked achromia and anisicytosis and poikilocytosis.

Both enucleated eyes were embedded in pyroxylin; examination revealed the picture of retinal glioma with formation of true and pseudorosettes, i. e., a neuroepithelioma. The differences in the two tumors were quantitative, not qualitative. There were the typical features of retinal glioma, namely, the darkly stained nuclei without visible protoplasm, densely packed in perivascular bands or cuffs. Between the cuffs of living cells were large masses of poorly stained necrotic cells, with hardly visible contours and small foci of calcification. In the left eye the tumor filled the vitreous cavity; in the right eye the tumor cells originated apparently in the layer of ganglion cells and in the inner nuclear layer and invaded the other layers of the retina and, in the posterior part of the globe, the choroid also. In the right eye the infiltration was of such degree that the normal retinal structure could hardly be ascertained. The cells were of the usual small round cell type, with almost no cytoplasm; the hyperchromatic nuclei were spherical, polygonal or wedge shaped. A small number of typical rosettes were distinguishable, a small radially arranged group of cells surrounding the central lumen. The lumen was circular in all sections, the groups of cells therefore representing small hollow spheres. The lumen was marked by a delicate refractile limiting membrane. Pseudorosettes were more numerous; the cells were arranged in short arcs or complete circles about clear spaces which were filled with fibrillar material. The optic nerves were not involved.

The left eye was enucleated at the age of 8 months. The right eye was treated with roentgen radiation; not only did the treatment fail to stop the growth, but the rapid progression of the tumor necessitated the removal of the second eye at the age of 11 months.

The mother of the child and the mother of the child in the next case were sisters. The family histories were entirely negative for glioma and for all other forms of malignant growth. Each child was the first and only child of the mother.

Case 2.—M. J. C., a girl aged 5 years, was admitted to the hospital with the complaint of vomiting, which, according to the mother was of projectile type. Since the vomiting had started, about one month before, the child had lost 3 pounds (1.3 Kg.) in weight. For one week before admission, the mother stated, the child had been vomiting everything she had eaten.

Physical examination revealed a blood pressure of 120 systolic and 80 diastolic. The child was well developed but thin; she appeared chronically ill but showed no evidence of dehydration. There was bilateral cervical adenopathy of slight degree. Tachycardia was present, with a pulse rate of 120 per minute. Examination of the thorax, abdomen, head and eyes revealed nothing abnormal. The Babinski sign was present bilaterally; Kernig's sign was absent.

The urine was normal. Studies of the blood revealed a hemoglobin content of 91 per cent; a red cell count of 4,700,000 and a white cell count of 5,800 per cubic millimeter, with 48 per cent polymorphonuclear leukocytes and 54 per cent normocytes and normochromic cells; a negative Widal reaction for typhoid and paratyphoid, a negative reaction for undulant fever, and a protein content of 19 Gm. per hundred cubic centimeters. A flat plate of the abdomen, after a barium sulfate enema, and a roentgenogram of the chest showed a normal condition. The Mantoux test gave a negative reaction to tuberculin in a dilution of 1:10,000, and the reaction to a dilution of 1:1,000 was negative after forty-eight hours.

Increased intracranial pressure was suspected, and a suboccipital decompression, with postoperative roentgenologic treatment, was performed. The child failed to improve. She did not talk; she ate well but vomited. She moved the left arm and leg only occasionally. The head, eyes, neck and lungs were normal. Tachycardia was noted. The right leg was spastic; the toes were extended and inverted at the ankle joint, and the right arm was spastic and rotated inward, with wrist drop. The abdominal reflexes were absent; the Babinski sign was present bilaterally; there was a knee clonus on the right, and the ankle jerks were absent.

On consultation with another brain surgeon, the diagnosis of left-sided subdural hematoma was persistently suggested, despite observations at the previous operation. For that reason a burr hole was made in the left frontal region. The dura was tense and did not pulsate. When the dura was opened a tense brain was exposed, without any evidence of subdural hematoma. A brain cannula was inserted, striking a dilated ventricle, and approximately 60 cc. of air was injected after a similar amount of ventricular fluid was removed in divided amounts.

Closure was carried out in the usual manner. Ventriculographic study showed a symmetric dilatation of the ventricular system up to the aqueduct, which was not visualized, a state presumably indicative of an expanding lesion of the brain stem. The condition

after the operation became progressively worse, and the child died thirty-six days after the second operation, or about four months after the initial symptoms were established.

Observations at Autopsy.—The body was that of an emaciated, 5 year old white girl in complete rigor mortis. The skin was pale, dusky and dry. No petechiae or jaundice was noted.

Head: The hair of the forehead was cut short; the hair over the back of the head had been shaved, and

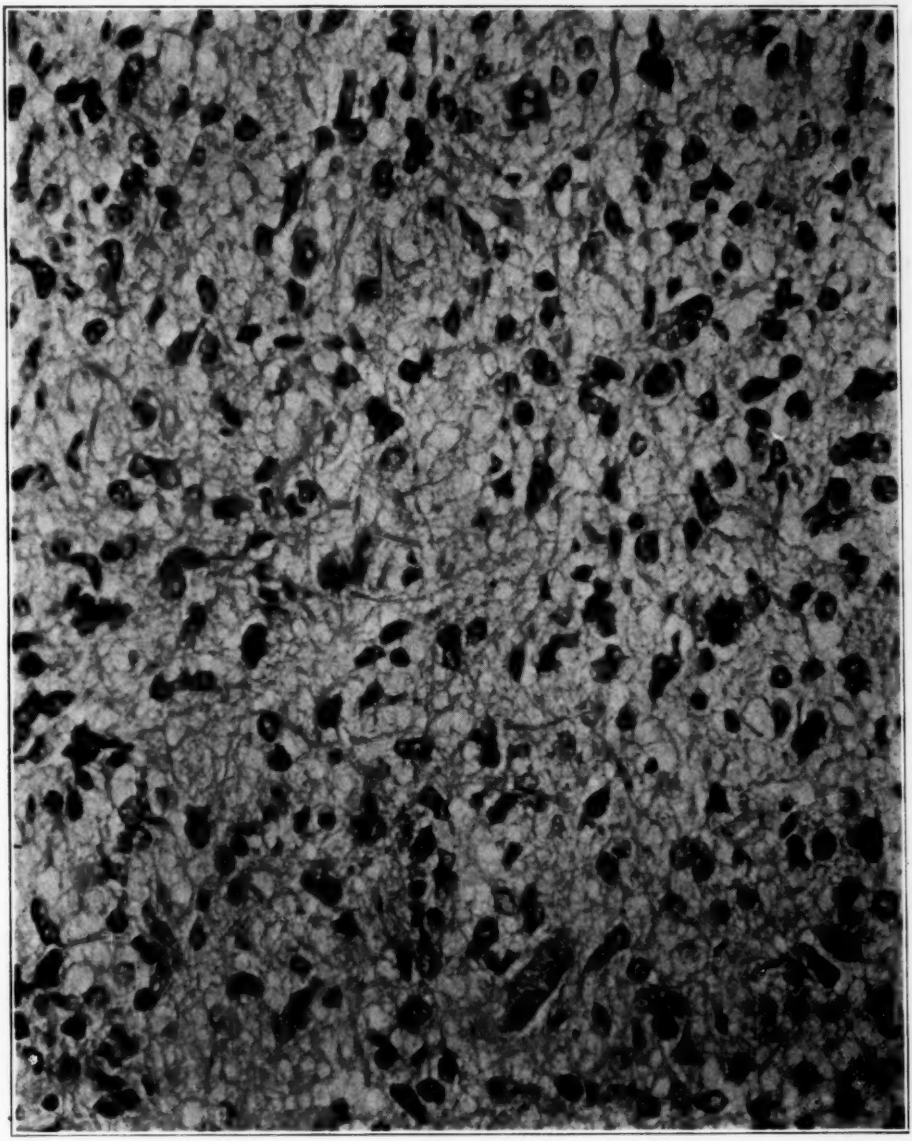


Fig. 1.—Section from the part of the brain tumor, exhibiting a fibrous stroma. Cell with round and oval nuclei and the interlacing character of the processes are clearly visible. Magnification, × 465.

here a semicircular, healed scar was noted. The head was large; the galea was not unusual. The bones of the calvaria were thin and translucent. Portions of both occipital bones were absent, having been removed at a previous operation. Also noted was a trephine opening in the lateral aspect of each parietal bone. When the skull was opened, the dura was found to be tense. The sinuses contained liquid blood; no thrombi were noted. The meninges were delicate; the gyri were flattened, and the sulci were narrowed and compressed. The brain appeared large. The pons and the brain stem anterior to it were the site of a whitish, club-shaped tumor, measuring 8 by 4 by 3 cm. The floor of the third ventricle had herniated and was thinned. When the corpus callosum was cut, an increased amount of clear cerebral fluid escaped. All the ventricles were greatly distended. The cerebral vessels did not appear unusual.

Chest: The thymus was small. Both pleural spaces were free of fluid and adhesions.

The heart lay free in the pericardial sac, which contained a small amount of clear, yellowish fluid. The epicardial surface was smooth and glistening. The endocardium was thin and smooth throughout. All the valves were thin and delicate. In the outflow tract of the left ventricle a subendocardial hemorrhage was

noted. The myocardium was reddish and of firm, muscular consistency. A few atheromatous plaques were noted in the ascending portion of the aorta, near the aortic valve. No developmental defects were noted.

Lungs: The lungs were fluffy and of cushion-like consistency. The pleura was smooth and grayish. On section, the parenchyma was noted to be aerated throughout and reddish. The bronchi and the pulmonary vessels were not unusual.

was paper thin and bulged outward. A notching due herniation through the incisura was seen. T aqueduct and the third and lateral ventricles show considerable dilatation.

On section, the pons and the mesencephalon appear swollen, owing to the infiltration of tumor, which w cystic and filled with greenish, soft, gelatinous materi the cyst was irregular in shape and had irregular peri eral extensions; it measured approximately 3 cm.

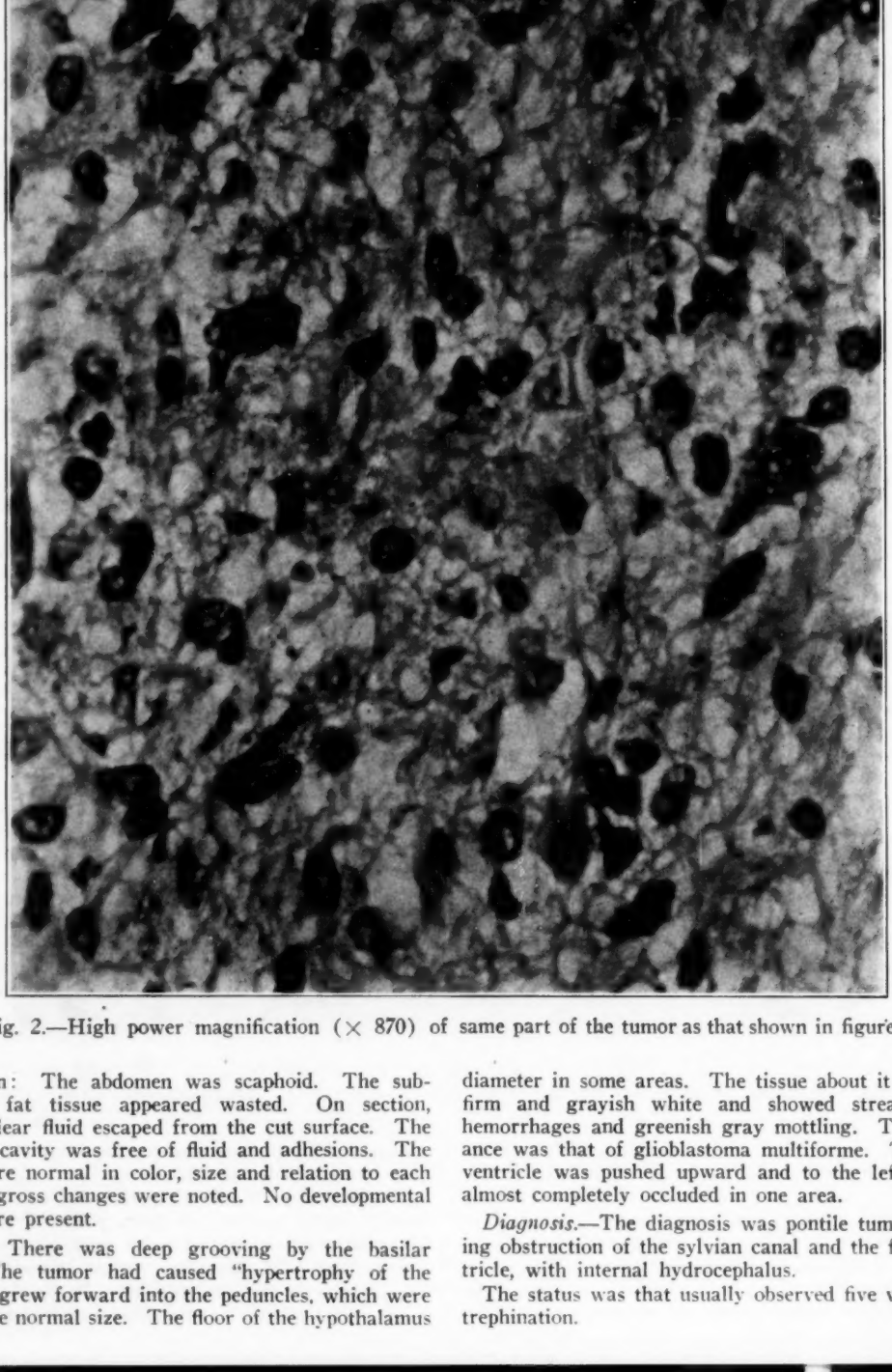


Fig. 2.—High power magnification (× 870) of same part of the tumor as that shown in figure 1.

Abdomen: The abdomen was scaphoid. The subcutaneous fat tissue appeared wasted. On section, drops of clear fluid escaped from the cut surface. The peritoneal cavity was free of fluid and adhesions. The organs were normal in color, size and relation to each other; no gross changes were noted. No developmental defects were present.

Brain: There was deep grooving by the basilar artery. The tumor had caused "hypertrophy of the pons" and grew forward into the peduncles, which were of twice the normal size. The floor of the hypothalamus

diameter in some areas. The tissue about it was sem firm and grayish white and showed streaky brow hemorrhages and greenish gray mottling. The appear ance was that of glioblastoma multiforme. The fourt ventricle was pushed upward and to the left and wa almost completely occluded in one area.

Diagnosis.—The diagnosis was pontile tumor produc ing obstruction of the sylvian canal and the fourth ven tricle, with internal hydrocephalus.

The status was that usually observed five weeks afte trephination.

Microscopic Examination of the Tumor (Dr. M. Tarlow).—The tumor was moderately cellular and presented cysts of variable size. The cells were fairly uniform in appearance and contained round or oval nuclei, in which there was chromatin of moderate amount. Nucleoli were absent. The rather fibrous stroma was composed of interlacing processes of the cells, which contained moderate amounts of cytoplasm. Even in preparations stained with hematoxylin and eosin the type cell was clearly revealed as the astrocyte. In some regions there was a tendency toward clumping of nuclei, and few true multinucleated cells were present. Mitotic figures did not occur. The margins of the tissue presented a few very large, well formed cells with abundant granule-containing cytoplasm and nuclei with nucleoli. These cells doubtless represented inclusion nerve cells. Areas of necrosis in which fantom cell forms were seen occurred in association with cysts. The walls of the cyst were formed of glia cells, frequently clearly visible as flattened astrocytes. A considerable number of rather thin-walled blood vessels was seen in certain portions of the cyst wall.

The tumor presented the characteristic features of a fibrous astrocytoma in which cyst formation had occurred.

COMMENT

The familial tendency of retinal glioma is well established. In the present cases pure coincidence certainly would not be sufficient to explain the occurrence of glioma duplex of the same histologic type, that of neuroepithelioma in 1 and of astrocytoma of the brain in the other, in children whose mothers were sisters. The occurrence of malignant growths of the same type in the retina and in the brain in collateral lines is presented for the first time; here, the females, themselves not affected, were the transmitters to a male (first case) and to a female (second case) child, respectively. Such observations are necessarily rare, for they usually escape attention. Even in these cases clinical observation and operative intervention failed to disclose the true picture, and only autopsy furnished the proper and indisputable evidence of the neoplasm of the brain. Without the permission for autopsy in the second case the bilateral glioma in the first child would necessarily be recorded as of sporadic occurrence.

The influence of heredity in mammary tumors of mice is one of the most widely studied subjects in connection with heredity and cancer in general. Inbred strains of mice of brother and sister matings have been under observation for more than fifty generations. Bittner [20] found that three influences, or inciters, in the occurrence of spontaneous tumors of the breast in mice are present, (*a*) the milk influence (extrachromosomal), transmitted by nursing; (*b*) hormonal stimulation, dependent on intrinsic or extrinsic factors, and (*c*) inherited susceptibility, which may be transmitted by males or females. The importance of the research cannot be overemphasized, but the work is hardly applicable to human cancer, which is seldom obviously hereditary. Broca, Wartkin and others reported on families with such a high incidence of cancer that it could hardly be attributed to chance alone. Roberts and Roberts reported the concurrent development of osteogenic sarcoma in 1 brother and 2 sisters, and Militzer [21] described simultaneously developing carcinoma in the same part of the stomach in identical twins 70 years of age. Hereditary susceptibility to cancer seems to become intensified in families in which the parents have the same type of cancer. Bauer's concept of a predisposition of certain organs to cancer was opposed by Ewing [22] and others, who stated the belief that either inherited susceptibility to cancer is negligible or there does not exist any specific hereditary predisposition in human cancer. It must be borne in mind, also, that cancer is not a disease entity and that even the establishment of a hereditary factor in one form of cancer would not permit generalization for all forms of cancer. According to Crabtree,[23] the incidence of fatal cancer in parents and siblings of white females with cancer of the skin is nearly twice the expectation on the basis of normal experience. For patients with cancer of the breast or cervix the familial incidence is more than one and a half times the normal expectancy. For males with cancer of the skin there is excessive familial incidence only in the cases in which the carcinoma develops at a relatively early age. The excessive familial incidence does not necessarily imply genetic factors, as cancer of the skin may be the result of environmental factors; cancers of the breast and cervix are more probably representative of hereditary origin. Waaler, in Norway, based his conclusion on 6,000 cases of carcinoma in which there appeared to be a hereditary predisposition of certain organs for malignant growths. Habs and Dietel cited an incidence of 8 per cent for carcinoma of the uterus in the twins of patients who were free of the tumor at death and of 34 per cent in the sisters of the afflicted

20. Bittner, J. J.: Observations on Genetics of Susceptibility for Development of Mammary Cancer in Mice, Cancer Research **2**:540, 1942; Possible Relationship of Estrogenic Hormones, Genetic Susceptibility and Milk Influence in Production of Mammary Cancer in Mice, ibid. **2**:710, 1942.

21. Militzer, R. E.: Carcinoma of the Stomach in Identical Twins, Am. J. Cancer **25**:544, 1940.

22. Ewing, J.: Heredity and Cancer, Bull. Am. Soc. Control Cancer **24**:4, 1942.

23. Crabtree, J. A.: Observations on the Familial Incidence of Cancer, Am. J. Pub. Health **31**:49, 1941.

patients; for carcinoma of the breast the figures were 16.5 and 44.7 per cent, respectively. Wood and Darling [24] presented the record of a family with frequent occurrence of bilateral carcinoma of the breast in four generations; an exception was a woman in the second generation, in whom the carcinoma developed in the cervix. The predisposition was transmitted through the maternal line of descent. Attention was drawn to this family during the study of the third generation, consisting of 3 sisters, all of whom had bilateral cancer of the breast. In 1 female of the fourth generation cancer of the breast developed at the age of 18. Cancer of the breast occurred only in those women who had been nursed by their mothers, a factor possibly analogous to the milk inciter of Bittner in mammary carcinomas in mice. There was no inbreeding in the family, and in the main line of descent only 1 of the fathers had carcinoma, in his case, of the colon; therefore a monohybrid recessive factor existed, causing semidominant inheritance within the family. A family with 5 sisters with mammary carcinoma, in 3 of whom the disease was bilateral, was reported by Handley. The observations of Bergen, Mayo and Giffin [25] included a study of 176 patients with proved cancer of the large intestine, in whose families the incidence of cancer was high. Forty-two per cent of the relatives had gastrointestinal cancer, as compared with 27 per cent of the two control groups. In their opinion, Bauer's concept of organ susceptibility is reasonable and warranted, as the offspring of persons with intestinal cancer had more often malignant growths of the intestinal tract than children both of whose parents were free of the disease. Conversely, Hanhart [26] could not determine a similar predisposition in his material, based on the study of descendants of 121 married couples, both of whom had cancer. Both partners of 33 of the 121 married couples had cancer of the stomach, and only 11 per cent of their children had a similar condition. Of the 121 couples, only 30 had children in whom cancer developed. A total of 590 children sprang of these marriages; the average expectancy of cancer for 286 of these offspring when past 50 years of age amounted to about 13 per cent, as compared with an expectancy of about 20 per cent for the population in general. Hanhart's study gave results much like those of investigations of twins, namely, the absence of a specific hereditary predisposition to cancer.

The scantiness of hereditary influences in human cancer is obvious when one considers the enormously high incidence of the ailment. Susceptibility to a certain degree may be transmitted by cancer of the breast from mother to daughter, but carcinoma of the prostate in the father does not predispose his daughter to any form of cancer. Human cancer is seldom obviously hereditary, like hemophilia, brachydactyly, polydactyly and color blindness. On the other hand, glioma and neurofibromatosis, within the group of malignant growths, are strikingly hereditary and therefore represent a distinct class in themselves.

The relatively large number of sporadic cases of glioma without familial tendency constitutes a point of controversy in establishment of the hereditary character of glioma. To the known cases of sporadic occurrence McCrea [27] recently added 12 (3 of bilateral and 9 of unilateral glioma), and I am adding 8 cases of unilateral and 1 case of bilateral glioma. This frequency of the sporadic form has led some authors to postulate a familial and a sporadic type of retinoblastoma, the latter the expression of somatic mutation. According to Best, the somatic mutation becomes hereditary, with a greater degree of penetration than in the previous generation. Weller emphasized that the person with retinoblastoma representing an apparent somatic mutation may become the originator of familial retinoblastoma if he survives and marries. One cannot fail to see the correctness of this assumption and may go even further and point out that the limited number of children of the present day urban population, together with the fact that many parents who have produced gliomatous offspring will refuse to have more children, or will refuse permission for enucleation of the second eye of a bilaterally affected child, helps to make the picture more obscure. Through the refusal to have more children or through the small number of children an apparent sporadic appearance obscures the possible existence of gliomatous fraternities through refusal of permission for enucleation of the second eye the life of the affected child falls short of the age of reproduction, and therefore the patient with apparent sporadic

24. Wood, D. A., and Darling, H. H.: Cancer Family Manifesting Multiple Occurrences of Bilateral Carcinoma of Breast, Cancer Research **3**:509, 1943.

25. Bergen, J. A.; Mayo, C. W., and Giffin, L. A.: Familial Trends in Human Cancer, J. Hered. **31**:511, 1940.

26. Hanhart, E.: Auffallend geringe Bedeutung der "Belastung mit Krebs" bewiesen durch das sehr häufige Freibleiben der Nachkommen aus 121 Ehen krebskranker Gatten im Kanton Glarus, Schweiz. med. Wchnschr. **73**:446, 1943.

27. McCrea, W. B. E.: Glioma of the Retina: A Review of Twelve Cases, Brit. J. Ophth. **27**:259, 1943

glioma does not become the founder of a family with vertical inheritance of the condition. Lenz pointed out that sporadic occurrence is the rule in the recessive type of inheritance and that the number of sporadic cases is necessarily greater with a small number of children. The tendency to inheritance of glioma apparently may be both dominant and recessive. In dominant inheritance the disease appears in the children when only one parent carries the trait, and usually about 50 per cent of the offspring are affected. In recessive inheritance, except for the sex-linked variety, both parents must carry the trait if the disease is to appear in any of their children; hence, the large number of cases of consanguinity associated with recessive inheritance. Most of the severe diseases are recessive and the mild ones dominant. The large number of gliomatous children within a fraternity and the apparent direct transmission through mother or father speak eloquently for a dominant single hereditary factor. The cases in which glioma is present in more than one generation with normal parents suggest a recessive mode of inheritance. According to Waardenburg,[28] consanguinity is often present in cases of glioma, which is contradictory to the observation of most authors, who have pointed out that the absence of consanguinity is evidence against the recessive mode of inheritance. The ratio of normal to affected children in most of the families indicates dominance, according to the figures of Franceschetti,[29] who found the ratio 63:77 for 25 families. Passow [30] expressed the belief that glioma shows a dominant or a recessive heredity; Clausen expressed doubt that dominant and recessive factors were present; he stated that glioma depends on one factor and is inherited through direct or indirect transmission and that some promoting or releasing factor, in addition to other elements, is essential. Hemmes concluded that not all the parents, children and siblings of his patients would be free from glioma if the disease were dominant; but, simultaneously, he ventured an opinion that the relatively rare incidence of consanguinity (in 3 of his 48 cases) spoke against the recessive mode. Nine patients with healed glioma of unilateral type were more than 25 years of age, 4 of them the parents of 9 healthy children. The 48 patients had 211 siblings over the age of 5 years, all of whom were free from glioma. The collateral lines were free; 24 patients with glioma had 76 siblings, who were parents of 281 unaffected children. Waardenburg concluded that both dominant and recessive inheritance is evident and that the cases of unilateral glioma suggest mediation of some disturbing influence in the hereditary mechanism, not hereditary somatic mutation. According to Aschoff and others, hereditary cytokinetic or somatokinetic disturbance plays a part. Badtke commented in connection with the mode of inheritance that the phenotypically normal are not necessarily genotypically normal and that only the careful watching of the offspring through many generations can furnish the answer. Best stated that mendelian laws do not apply to glioma and assumed that an unknown, but hereditarily established, derangement is present.

Griffith and Sorsby suggested that hereditary glioma represents a distinct histologic entity which differs from the sporadic variety, the exciting or inhibitory factors not necessarily being genetic, since environmental as well as genetic factors may suppress or make manifest the given genetic tendency. According to their opinion, gliomatous fraternities with unaffected antecedents are suggestive of recessive inheritance, but the incidence of 47.8 per cent, as against the theoretic incidence of 25 per cent, together with the absence of consanguinity, speaks against the recessiveness of the trait. Glioma in direct transmission was evident in 28 pedigrees (an incidence of 61.1 per cent in 19 available complete sibships). Genetic analyses show dominance, though irregular in type, as gliomas occurred in children of parents of an affected stock who were themselves unaffected.

The available data furnish no clearcut evidence that the factor or factors determining the heredity of glioma behave as does either a simple mendelian dominant or recessive trait. This confused picture suggests that a possible somatic variation, probably a structural anomaly of the retina, is inherited and that on this basis retinoblastoma may or may not develop. The hereditarily determined somatic variation, according to Weller, is capable of varying degrees of intensity. Simple mendelian recessive defects of the retina are known to occur in the mouse (Keeler) and the rat (Bourne, Campbell and Tausley); furthermore, Weller cited the occurrence with glioma of coloboma of the iris (Wintersteiner) and of small malformations, even very small tumors (Fuchs), and the obser-

28. Waardenburg, P. J.: Das menschliche Auge und seine Erbanlagen, Haag, M. Nijhoff, 1932.

29. Franceschetti, A.: Die Vererbung von Augenleiden, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 1, p. 476.

30. Passow, A.: Hereditäre Augenerkrankungen, das Gliom der Netzhaut, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 16, p. 934.

vation of Ch'in concerning the overlapping of malformation and neoplasm as examples of presumptive preblastomatoid lesions. The changes in the opposite eye, the retrogression of glioma, suggest such structural deviations, as do the changes in neurofibromatosis and tuberous sclerosis, which represent developmental lesions rather than true neoplasms. Retinoblastoma apparently belongs to the same group, conditions which have a hereditary basis and originate from lesions intermediate between developmental disturbances and true neoplasms.

SUMMARY

The hereditary basis of malignant growths, especially that of retinoblastoma, is evaluated with reference to horizontal, vertical and collateral inheritance in the family history, and the importance of research on twins is stressed.

A case of glioma of the retina and 1 of glioma of the brain occurring in collateral lines, hitherto undescribed, are reported.

31 Lincoln Park.

INJECTION OF OXYGEN INTO TENON'S CAPSULE

MAJOR HAROLD G. SCHEIE
AND
LIEUTENANT COLONEL PHILIP J. HODES
MEDICAL CORPS, ARMY OF THE UNITED STATES

Injection of contrast mediums into Tenon's capsule, as described by Spackman,[1] has proved invaluable in the localization of intraocular foreign bodies. This is especially true of the type of injury incurred in jungle warfare, in which hand grenades, booby traps and small antipersonnel mines are used extensively. These usually cause multiple, small, penetrating wounds, containing opaque foreign bodies of varying sizes, which roentgenographically look like "snow flurry" collections of opaque debris. When the region of the eye is involved, it is frequently impossible to distinguish intraocular foreign bodies from those outside the eyeball by any procedure except roentgenographic study with injection of a contrast medium into Tenon's capsule (fig. 1). This method is also of considerable assistance in the localization of foreign bodies lying near the limits of the globe and in diagnosing double perforations of the eyeball.

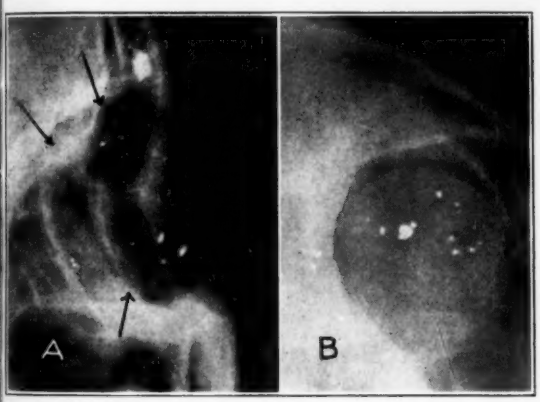


Fig. 1.—Multiple intraocular mortar fragments localized by air studies of Tenon's capsule.

Early in our experience injections of air were made into Tenon's capsule. About 6 cc. was injected into the capsule, after which stereoscopic roentgenograms were obtained without the Bucky diaphragm in the posteroanterior and lateral projections (fig. 1). While the procedure was diagnostic and enabled one to localize intraocular foreign bodies, it made hazardous any surgical intervention soon after the injection. This was especially true when the anterior chamber had to be opened, as for the removal of a foreign body by the anterior route or for linear extraction of a traumatic cataract or, at times, for the simultaneous performance of these two procedures. The air in Tenon's capsule exerted external pressure on the eyeball, increasing the incidence of loss of vitreous and prolapse of the iris. Because of this, carbon dioxide and then oxygen, both known to be absorbed more rapidly than air from tissues or closed spaces, were tried in an effort to minimize the dangers of increased extraocular pressure at operation.

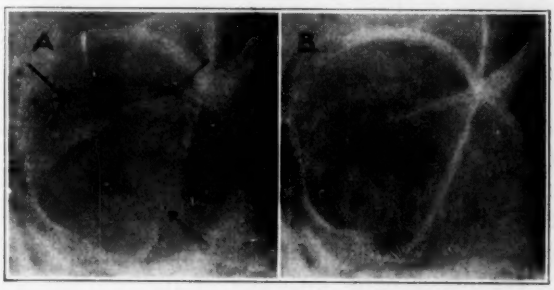


Fig. 2.—Injection of oxygen into Tenon's capsule. *A*, roentgenogram made immediately after injection; *B*, roentgenogram four hours after injection, revealing considerable absorption of oxygen.

In our experience, air injected into Tenon's capsule was not absorbed completely for three to four days. Most of the air could still be seen at the end of twenty-four hours, disappearing slowly thereafter. Carbon dioxide, on the other hand, was absorbed too rapidly to be effective as a contrast medium. Decreasing amounts of the gas were noted between the first and the last exposure of a routine roentgenographic study. When, for technical reasons, the examination had to be repeated, there was barely enough carbon dioxide in Tenon's capsule to outline the globe.

1. Spackman, E. W.: X-Ray Diagnosis of Double Perforation of Eyeball After Injection of Air into Space of Tenon, Am. J. Ophth. **15**:1007-1012 (Nov.) 1932.

Oxygen proved to be an ideal gaseous agent. It produced excellent visualization of the globe and was absorbed slowly enough to permit reexamination when necessary; yet the oxygen was absorbed fast enough to avoid the risk of vitreous escaping at operation. Most of the oxygen was absorbed within four to eight hours, though a slight amount could still be visualized twenty-four hours after the injection (fig. 2).

The technic described by Spackman [1] for injecting air into Tenon's capsule was used (fig. 3). A curved no. 25 needle attached to a 10 cc. syringe was employed. The eye was turned downward and inward by a fixation forceps and the needle inserted approximately 5 to 6 mm. behind the limbus, the point proceeding subconjunctivally for a few millimeters, in the upper outer quadrant of the eye, before entering Tenon's capsule. The oxygen was introduced slowly and in successful injection immediately produced proptosis. Approximately 6 cc. of oxygen produced adequate visualization.

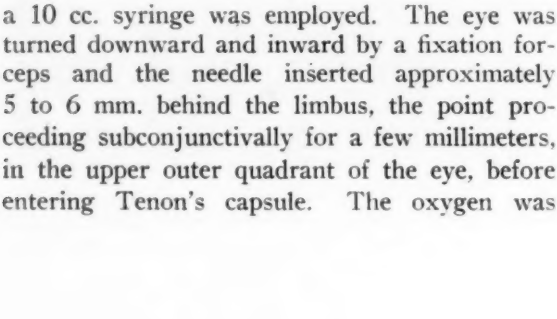


Fig. 3.—Injection of oxygen into Tenon's capsule. *A*, manner in which the eye is fixed and the needle is inserted; *B*, appearance of the eye before injection; *C*, appearance of the eye immediately after injection of 6 cc. of oxygen. Note the cataract in the injured eye.

The oxygen was obtained from an ordinary oxygen tank with a sterile rubber tube which contained a cotton filter. The oxygen was allowed to flow through the tubing for several seconds, after which it was introduced directly into the barrel of the syringe through the point for attachment of the needle, displacing the plunger as it entered the barrel. The needle was then quickly applied and the injection carried out.

Griffin, Gianturco and Goldberg [2] described a stereoscopic method for localizing intraorbital foreign bodies in which a semiopaque artificial eye was used to outline the globe. We compared this procedure with injections of air into Tenon's capsule to see how often the image of the artificial eye coincided with the contour of a patient's eye delineated with air. The major portion of the artificial eye invariably was superimposed on the patient's eye. Their outer margins, however, usually did not coincide. Enough discrepancy existed to convince us that, in our hands at least, the artificial eye was of limited value in localizing foreign bodies lying within several millimeters of the sclera.

3400 Spruce Street.

2. Griffin, E. P.; Gianturco, C., and Goldberg, S.: A Stereoscopic Method for Localization of Intraorbital Foreign Bodies, Radiology **40**:371-374 (April) 1943.

CLINICAL STUDY OF EFFECT OF TOBACCO ON THE NORMAL ANGIOSCOTOMA

AUSTIN I. FINK, M.D.
Assistant Resident in Ophthalmology, Long Island College Hospital
BROOKLYN

In 1926 the classic form of the angioscotoma was first described.[1] This work has been a source of aid to clinicians investigating disease of the nasal accessory sinuses,[2] forms of edema,[3] glaucoma[4] and menstrual disturbances.[5] The research worker, too, has had recourse to angioscotometry in studying the effects of sulfanilamide,[6] inhalation of oxygen,[7] and amphetamine sulfate,[8] and studies of the effects on the visual fields of high altitude[9] have been a basis of investigations in World War II. No effort has been made, however, to determine the effect of smoking on the normal angioscotoma. Since tobacco smoking is so widespread, it was thought that knowledge of its effect might be of clinical and experimental value. It was therefore decided to study the effect on the central visual fields of smoking 1 cigaret with inhalation.

Read at a meeting of the Brooklyn Ophthalmological Society April 19, 1945.

From the Department of Ophthalmology of the Long Island College of Medicine and the Long Island College Hospital.

1. Evans, J. N.: A Preliminary Report of the Retinal Vessel Scotoma, Am. J. Ophth. **9**:118-119 (Feb.) 1926.

2. Evans, J. N.: Application of Angioscotometry to the Study of Nasal Accessory Sinus Disease, Ann. d'ocul. **169**:717-730 (Sept.) 1932.

3. Evans, J. N.: The Scotometry of Retinal Edema, Am. J. Ophth. **16**:417-424 (May) 1933.

4. Evans, J. N.: Transient Fluctuations in the Scotoma of Glaucoma, Am. J. Ophth. **18**:333-347 (April) 1935.

5. Evans, J. N.: A Scotoma Associated with Menstruation, Am. J. Ophth. **24**:507-519 (May) 1941.

6. Rosenthal, C. M.: Changes in Angioscotomas Associated with the Administration of Sulphanilamide, Arch. Ophth. **22**:73-81 (July) 1939.

7. Rosenthal, C. M.: Changes in Angioscotomas Associated with the Inhalation of Oxygen, Arch. Ophth. **22**:385-392 (Sept.) 1939.

8. Rosenthal, C. M., and Seitz, C. P.: Alterations in Angioscotomas Following the Oral Administration of Benzedrine Sulphate, Am. J. Ophth. **23**:545-549 (May) 1940.

9. Evans, J. N., and McFarland, R. A.: Effects of Oxygen Deprivation on Visual Fields, Am. J. Ophth. **21**:968-980 (Sept.) 1938.

METHODS AND MATERIAL

Angioscotometry was the method used in plotting the central visual fields. The word "angioscotoma" signifies a "defect of the visual fields resulting from the blind spot of Mariotte and related in form to the pattern of distribution of the retinal vessel tree."[1] The shadows, after extensive research, have been interpreted as arising through modifications in the functions of the retinal perivascular spaces[10] and in the retinal synaptic junctions.

Technic.—The scotoma was mapped by the method advocated by Evans.[11] The defects in the visual fields could thus be studied both qualitatively and quantitatively.

Both the Evans and the Lloyd stereocampimeter and charts were used. Monocular fixation was employed throughout the experiment. The subject was permitted to rest for approximately ten minutes before the actual mapping was begun. He indicated the disappearance of the test object by tapping with a pencil or by saying "gone." The diameters of the test objects used ranged from 0.4 to 0.6 mm. Illumination of the test chart was approximately 15 foot candles. The blindspot of Mariotte was outlined. Then the two main superior angioscotomas were plotted, care being taken at all times to move the test object at right angles to the border of the defect.

Subjects.—When this work was begun, a series of 8 subjects were studied merely for the qualitative effect, in order to become familiar with the characteristics of the anticipated changes. When, after study of this series, it became evident from the results obtained that inhalation of tobacco produced an effect on the visual fields, a series of 6 subjects were studied quantitatively, the time, blood pressure and pulse rate being correlated with the changes in the field defect. The ages of the subjects ranged from 17 to 28 years. No subject was chosen unless he or she inhaled while smoking. The extent of the habit in the subjects varied from 3 to 20 cigarets per day. Each subject had had a physical examination at least six months prior to the time that the test was made and had been found to be in good health.

Procedure.—At the time the test was made the subject had not smoked for at least one and one-half hours. He rested for approximately ten minutes before any mapping was begun. During this period the pulse and the blood pressure were recorded. The subject was familiarized with the apparatus and instructed to respond either by tapping with a pencil or by saying "gone."

10. Evans, J. N.: Angioscotometry, Am. J. Ophth. **9**:489-506 (July) 1926; footnote 1.

11. Evans, J. N.: Clinical Scotometry, New Haven, Conn., Yale University Press, 1937.

The first map, or control, was then plotted. The subject was then given a popular brand of cigaret (one brand being used exclusively), and 40 mm. of it was smoked. He inhaled as frequently as was his habit at other times. A second chart was plotted immediately after the smoking, and the pulse and blood pressure were recorded. The same technic was employed at fifteen to twenty minute intervals until the control stage was again reached.

RESULTS

The accompanying charts and tables illustrate the results obtained. They show clearly that inhalation of 1 cigaret increased the area of the angioscotoma. There was no change in the area of the blindspot. Pupillary changes were not detectable by available methods. The first effects were noted (table 1) from two to twenty minutes after smoking. The average time was nine minutes. Maximum effects were obtained from seventeen to forty minutes after the last inhalation. The average time was twenty-four minutes. In sixty to one hundred and seven minutes the effect was completely gone. The average time was seventy-eight minutes.

The effect on the blood pressure did not vary more than 2 to 5 mm. of mercury. Whereas the changes in blood pressure were negligible for all subjects, the pulse rate increased as much as 24 beats per minute in 1 subject. The greatest increase in the pulse rate corresponded in time to the most pronounced changes in the angioscotoma. The fields in figure 1, plotted according to the method used by Evans [11] for mapping scotomas, are those of T. G., a 24 year old medical student. His general physical and ocular status was apparently normal, as demonstrated by a complete Army physical examination one month prior to the test. The habit of smoking was well established with the subject. He smoked

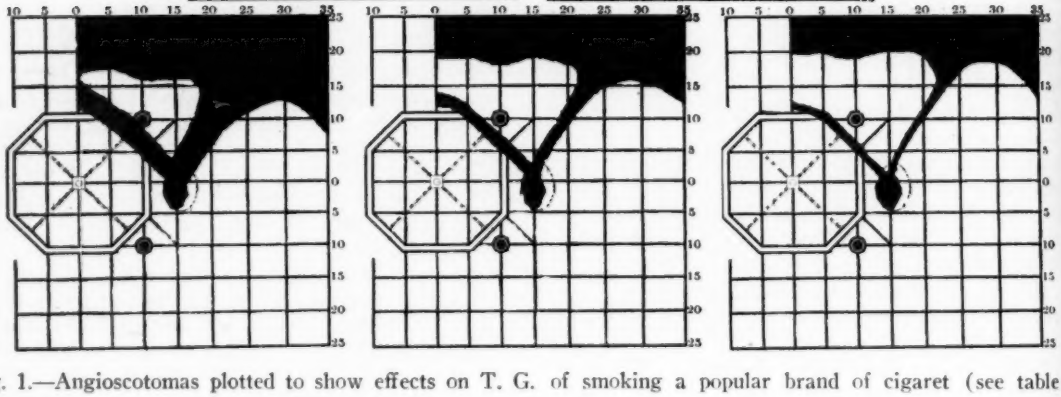


Fig. 1.—Angioscotomas plotted to show effects on T. G. of smoking a popular brand of cigaret (see table 2

TABLE 1.—*Appearance and Duration of Changes in the Scotoma Produced by Smoking a Popular Brand of Cigaret*

Subject	First Change, Min.	Maximum Effect, Min.	Effect Lost, Min.
G. F.	15	25	65
C. B.	2	17	107
V. K.	5	20	65
T. G.	3	18	61
C. S.	20	40	91
Average	9	24	78

TABLE 2.—*Effects of Smoking a Popular Brand of Cigaret on Subject T. G.*

Time	Blood Pressure	Pulse	Scotoma Units
8:25	120/68	86	95
8:45	118/74	98	153
9:00	120/76	88	182
9:25	120/76	86	124
9:43	120/80	80	95

verage of 20 cigarets a day. He had not smoked or two hours previous to the time the test was erformed. The data appear in table 2. No ntoward effects were noted.

COMMENT

Angioscotomas, as stated previously, apparently represent modifications in the functions of the retinal perivascular spaces. It is established that nicotine, the principal drug of tobacco, produces generalized peripheral vasocontriction.[12] Nicotine is thought to exert its vascular effect through stimulation of the sympathetic nervous system, causing an increased output of epinephrine in the body. Because of this, one would expect to find a decrease in the area of the angioscotoma. Instead, widening, rather than a narrowing, was produced. There are two possible explanations for this apparent paradox: First, "Contractions of the fibers of the astrocytes, which send footplates to form the wall of the perivascular space, also increase the amount of fluid within the space by virtue of the greater cross section thus created [page 152]."[11] Second, it is recognized that synaptic junctions, which are very sensitive to deleterious agents, may act as a fuse to protect the layer of rods and cones. Therefore, any interfering influence could be a factor in the production of defects in the visual fields. Since nicotine has been shown to alter the conductivity at synaptic junctions,[11] it would not be unreasonable to assume that this disturbance may contribute to the alteration of the angioscotoma. To summarize, then, any one or a combination of the two factors might explain the widening of the angioscotoma found in this experiment. At present studies are being conducted in the department which are expected to elucidate the matter.

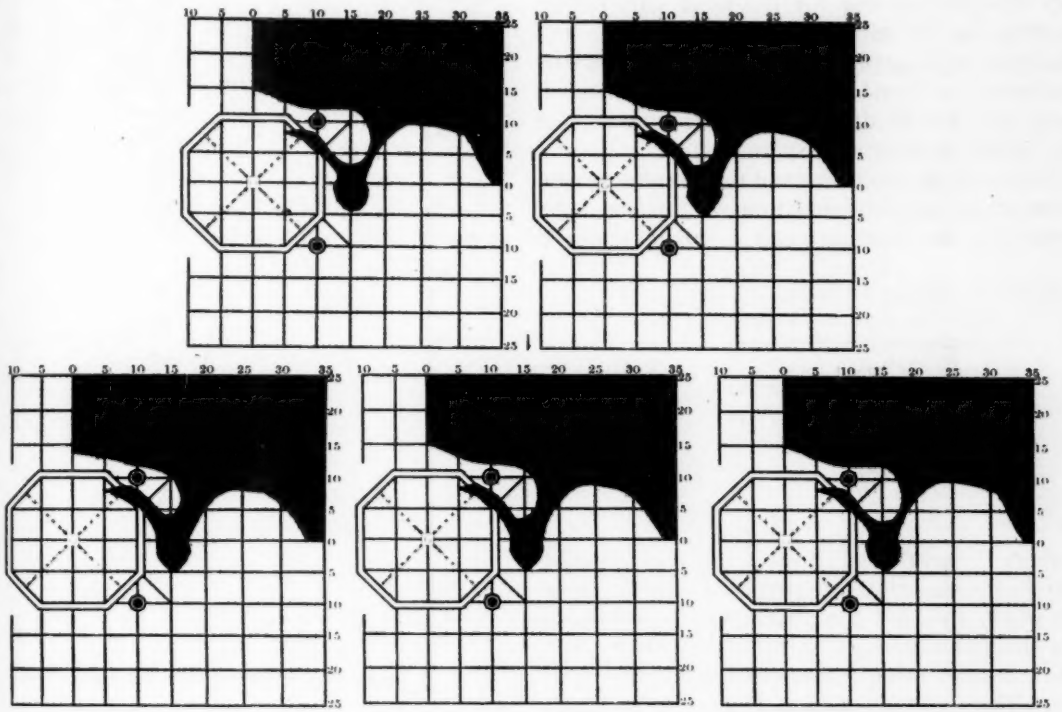


Fig. 2.—Angioscotomas plotted to show effects on T. G. of smoking a cigaret of low nicotine content (see table 3).

One may speculate as to the nature of the elements found in tobacco in an attempt to understand the results obtained. Essentially, three principal constituents of tobacco must be taken into consideration: (1) nicotine, (2) tars and resins and (3) foreign protein.

It has been believed that the foreign protein taken into the body through the mucous membrane of the respiratory tract in the act of inhalation might explain the effects of tobacco on the human circulation. However, Herrell and Cusick,[13] who studied vascular and retinal abnormalities following the inhalation of tobacco

12. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941.

13. Herrell, W. E., and Cusick, P. L.: Vascular and Retinal Abnormalities Following Inhalation of Tobacco Smoke, Proc. Staff Meet., Mayo Clin. **13**:273 (May 4) 1938.

smoke, concluded that the effects produced were not related to "an allergic phenomenon or a phenomenon of sensitivity."

Tars and resins have also been suspected by some investigators[14] of causing the circulatory changes produced by inhalation of tobacco. Weatherby[15] and Main[16] demonstrated very different circulatory alterations with tobacco of high and low nicotine contents while the other two factors (proteins and tars and resins) were kept constant. Haag and Larson[17] obtained similar results.

From the evidence presented, it would not seem unreasonable to conclude that the circulatory changes are due for the most part to the nicotine content of the tobacco. The same explanation may apply to the alterations in the angioscotoma found in the present experiment, which are due to alterations in the functions of the retinal perivascular spaces.[10]

In an attempt to understand the circulatory and vascular effects of inhalation of tobacco with respect to the nicotine content, many research

TABLE 3.—*Effects of Smoking a Cigaret of Low Nicotine Content on Subject T. G.*

Time	Blood Pressure	Pulse	Scotoma Units
8:00	120/76	82	207
8:10	122/76	82	216
8:25	120/78	84	221
8:35	120/74	80	216
8:45	122/78	80	207

workers[18] have used tobacco of low nicotine content for experimental purposes. In the present work, too, for completeness of controls, it was thought necessary to carry out angioscotometric studies using tobacco of low nicotine content. Through the kindness of Dr. H. B. Haag, of the Medical College of Virginia, it was possible to obtain special cigarets containing 0.2 per cent nicotine by weight. The average popular brand of cigaret contains 2 per cent nicotine.[17]

In this second series, the subjects were the same persons who had volunteered for the quantitative studies with the popular brand of cigaret. They were not informed that the cigarets were low in nicotine content. The method, technic and procedure employed were identical with those described for the experiment with cigarets high in nicotine. The results indicated (fig. 3 and table 4) that cigarets containing only 0.2 per cent nicotine by weight also produced a wide

TABLE 4.—*Appearance and Duration of Changes in Angioscotoma Produced by Smoking a Cigaret of Low Nicotine Content*

Subject	First Change, Min.	Maximum Effect, Min.	Effect Lost, Min.
G. F.	2	2	18
C. B.	2	2	32
V. K.	2	2	43
T. G.	10	25	45
O. S.	5	5	20
Average	4	7	32

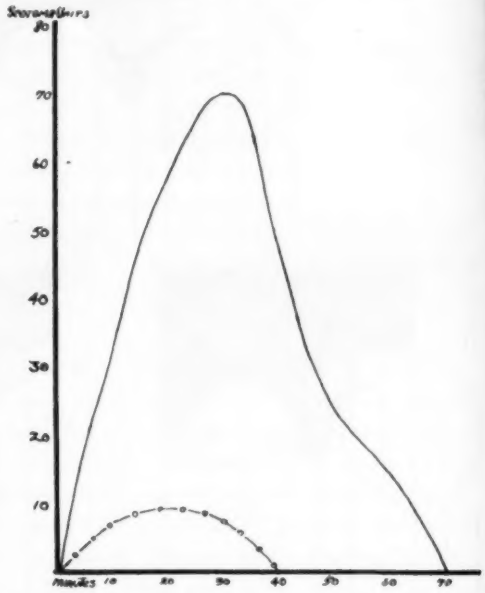


Fig. 3.—Effects of inhalation of tobacco, expressed i scotoma units. The solid line indicates effect of smokin a popular brand of cigaret, and the line with circle the effects of smoking a cigaret of low nicotine conte

ing of the angioscotoma. However, the altera tion resulting from the inhalation of these cigaret was much less than that produced when th popular brand of cigarets was employed. Th first effects were noted within two to ten min utes after the last inhalation. The average tim was four minutes. Maximum effects were ob tained in two to twenty-five minutes. The averag time was seven minutes. Eighteen to forty-fiv minutes after smoking the effect was completel gone. The average time was thirty-two minute The effects on the blood pressure and the puls rate did not vary appreciably.

From these studies on cigarets of low nicotin content it is possible to draw the followin

14. Evans, W. F., and Stewart, H. J.: The Effect of Smoking Cigarettes on the Peripheral Blood Flow, Am. Heart J. **26**:78-91 (July) 1943.

15. Weatherby, J. H.: Skin Temperature Changes Caused by Smoking and Other Sympathomimetic Stimuli, Am. Heart J. **24**:17-30 (July) 1942.

16. Main, R. J.: Acute Effects of Smoking on Respiration and Circulation, Proc. Soc. Exper. Biol. & Med. **48**:495-500 (Nov.) 1941.

17. Haag, H. B., and Larson, P. S.: Some Chemical and Pharmacological Observations on "Low Nicotine" Tobacco, Science **97**:187-188 (Feb. 19) 1943.

18. Main.[16] Weatherby.[15] Haag and Larson.[17]

conclusions: 1. Cigarets containing one-tenth the nicotine content of the popular variety are associated with a widening of the angioscotoma. 2. The degree of widening resulting after inhalation with cigarets of low nicotine value was less than that which occurred when the popular brand was employed. One may assume from these observations that differences in the nicotine content of cigarets result in varied degrees of widening of the angioscotoma, provided all the other factors remain equal.

A final control was thought necessary in order to determine whether the act of inhalation itself was the dominating factor in the alteration of the angioscotoma found in this experiment. The subject was asked to inhale an unlighted cigaret for eight minutes. This time limit was arrived at by taking into account the average time previously required to smoke the desired length of the popular brand of cigaret or the cigaret low in nicotine content. The subject inhaled as often as he had been accustomed to while smoking a lighted cigaret. The results showed that in a series of 5 subjects no alteration of the angioscotoma was recognized.

CONCLUSIONS

Under the conditions of these experiments and with the subjects tested the following conclusions were arrived at:

1. The smoking of a certain popular brand of cigaret produces a widening of the angioscotoma.

2. Cigarets containing one-tenth the nicotine content of the popular variety produce an alteration of the angioscotoma of lesser degree than that observed with the popular brand.

3. The controlled inhalation of an unlighted cigaret produced no alteration of the angioscotoma.

It would seem fair to postulate that the effect on the angioscotoma was brought about by changes in the sympathetic hormonal mechanism due to the presence of the nicotine.

Long Island College Hospital.

CYCLODIATHERMY IN TREATMENT OF GLAUCOMA DUE TO RUBEOSIS IRIDIS DIABETICA

ANDREW DEROETTH, M.D.
SPOKANE, WASH.

Rubeosis iridis diabetica is one of the most disastrous ocular diseases, for it usually involves both eyes and, with rare exceptions, causes uncontrollable glaucoma. In none of the 32 cases of this disease found in the literature could miotics control the tension. Surgical procedures, such as iridectomy (Arruga[1]), iridencleisis (Kurz[1]), trephination (Motolese,[1] Gallino,[1] Kurz,[1] Fehrmann,[1] Sugar[1]), cyclodialysis (Salus[1]) and posterior sclerotomy (Fehrmann[1]), were useless, or even disastrous. The intolerable pain caused by glaucoma necessitated enucleation in several cases. Fralick,[1] in his excellent and comprehensive paper on this subject, reported on the removal of 4 eyes in 3 cases of diabetic rubeosis iridis. Any attempt to save a fraction of the vision, or even the eyeball alone, is worth while in a case of this desperate condition. In the 2 cases reported here cyclodiathermy was performed with the latter purpose.

REPORT OF CASES

CASE 1.—Mrs. J. H., aged 28, a housewife, had the onset of diabetes at the age of 13 years. When the diabetes was first discovered, she required 70 units of insulin with a maintenance diet. Her condition improved with management, so that by the end of the first year she was taking only 24 units of insulin a day. At the age of 17 years she had acidosis, which required hospitalization. At the age of 21 the insulin was changed to protamine zinc insulin, and she required 30 units to control her diabetes. She had acute nephritis in February 1944. In January 1945 her blood pressure was 190 systolic and 110 diastolic. Urinalysis gave a 3 plus reaction for albumin, 34 mg. of urea per hundred cubic centimeters, no acetone and 1.3 per cent of diacetic acid. The blood sugar measured 180 mg. per hundred cubic centimeters when she was receiving 30 units of insulin and 100 mg. when she was receiving 40 units, with a diet of 150 Gm. of carbohydrate, 70 Gm. of protein and 100 Gm. of fat.

She came for examination of the eyes a few times after the age of 19 years; vision was normal with a correction of —0.5 D. There was no pathologic condition of the fundus in January 1942. On June 1, 1944 she stated that she had had failing vision for four months. Vision was 20/200 in each eye; with a correction of —0.50 D. cyl., axis 78 it was 20/66. Both fundi showed copper-colored arteries, very large veins and capillaries and numerous small retinal hemorrhages.

On Nov. 21, 1944 vision in the right eye was limited to counting fingers at 2 feet (60 cm.) and was 20/[illegible] in the left eye. Tension was 80 mm. (Schiøtz) in the right eye and 22 mm. in the left eye. Both disks were almost entirely covered with a thin veil of connective tissue, which extended beyond their margins. Many vessels were sheathed. There was a hemorrhage into the vitreous below the left disk. A network of vessels was present in the upper nasal section of the pupillary portion of the iris of the right eye. In another week a full picture of rubeosis iridis had developed in the right eye. On the lesser circle of the iris there was a reddish flush, produced by numerous new capillaries. Two large vessels and several finer ones radiated from the ring of capillaries to the base of the iris and disappeared behind the limbus. The pupil was round, measured 3 mm. in diameter and was fixed to light. There was a hemorrhage in the vitreous of the right eye.

On Dec. 8, 1944, the left iris showed a fine capillary ring in the lesser circle, and tension was over 80 mm. of mercury in each eye. There was no perception of light in the right eye, and vision in the left eye was limited to perception of hand movements. Pilocarpine, neostigmine, cocaine and epinephrine, and drops of eucatropine were tried, but without effect on the tension or on the pain. The cornea of the right eye became smoky, and sometimes, with the eye stone hard, the pain was unbearable.

On Feb. 9, 1945 there was no perception of light in either eye. Perforating cyclodiathermy was performed around the upper half of the cornea of the right eye and three weeks later around the lower half. The Walker apparatus was employed, using a Weve needle with a 1 mm. point, and fifty-five punctures were made 2 to 6.5 mm. from the limbus, with a current of 2 milliamperes. The pain disappeared immediately after the operation, and tension was 20 mm. four weeks later. The left eye became stone hard. On March 21 cyclodiathermy was performed on the left eye in the sector between 2 and 8 o'clock. There has been no pain in either eye since the operation.

At the time of this report, on June 9, there is no perception of light in either eye. Tension is 9 mm. in the right eye and 60 mm. in the left eye. On Dec. 3, the right eye was slightly shrunken; the tension of the left eye was 9 mm. The right eye has a shallow anterior chamber, a wide pupil and an atrophic iris, with ectropion uveae. With the slit lamp, only a few small vessels are visible in the iris. There are numerous small vessels immediately behind the lens; evidently a hemorrhage in the vitreous is in the stage of organization. The left eye has a normal anterior chamber and a few small vessels in the iris. The pupil is of medium width and shows a weak grayish red reflex. Gonioscopic examination reveals complete blocking of the angle in each eye.

1. For the literature on rubeosis iridis diabetica, see Fralick, F. B.: Rubeosis Iridis Diabetica, Am. J. Ophth. **28**:123, 1945.

CASE 2.—Mr. F. S., aged 20, who had had diabetes for twelve years, consulted me on Sept. 11, 1941, because of severe retinopathy. In March 1942 rubeosis iridis was noted, and tension was 56 mm. in the right eye and 65 mm. in the left eye. Vision in each eye was limited to counting fingers at 1.5 meters. In April 1942 iridectomy and iris inclusion were performed on each eye because of tormenting pain. The tension fluctuated but was high again in June 1942. On June 27, 1942 there was no perception of light in either eye. Nonperforating diathermy, with a current of 50 milliamperes, was performed on the upper half of each eye. On Sept. 10, 1942 examination showed a shallow anterior chamber, a large pupil, ectropion uveae and a grayish red haze in the vitreous of each eye. Tension was well below normal. On Aug. 3, 1943 both eyes showed advanced atrophy of the eyeball, a shallow anterior chamber, opacity of the lens and atrophy of the iris.[1a]

COMMENT

Cyclodiathermy was eminently advocated for hemorrhagic glaucoma due to thrombosis of the central retinal vein by Vogt [2] and by Albaugh and Dunphy.[3] The latter used their modification of cyclodiathermy (nonperforating), among others, in 6 cases of diabetes; 5 of these were cases of hemorrhagic glaucoma, and in 4 eyes the tension was controlled with the operation. None of these authors mentioned having used the method in a case of rubeosis iridis. Meyer and Sternberg [4] performed the cyclodiathermy as described by Vogt in an undisclosed number of cases for glaucoma associated with rubeosis iridis diabetica. "Freedom from pain nearly always occurs within thirty-six hours following surgery."

Scobee [5] performed cyclodiathermy with success in a case of rubeosis iridis. In a man aged 31 who was suffering from uncontrolled diabetes and retinopathy rubeosis iridis and glaucoma developed in the right eye. Iridencleisis did not reduce the tension; so cyclodiathermy was done. Seven weeks after operation the tension was 25 mm. Twenty-three months later the eye was slightly shrunken and painless. Guerry [6] treated 1 eye with this condition (the right eye in case 3) by means of his novel operation, angiodiathermy, and cyclodiathermy, with the result that the tension was too low to be measured in the fourth postoperative week. In performing angiodiathermy he coagulates one of the long posterior ciliary arteries just anterior to its entrance into the sclera.

As to the extent of cyclodiathermy in cases of hemorrhagic glaucoma, I quote Albaugh and Dunphy:

> . . . We now believe that in this type [hemorrhagic] of glaucoma a cyclodiathermy of any less than one-half the globe is more often than not insufficient.

However, in my second case, the surface diathermy was used only around one-half the cornea in each eye, and the result was atrophy of the eyeballs. It is possible that the diathermic coagulation included the main branches of both the nasal and the temporal long posterior ciliary artery. There is convincing experimental evidence that atrophy of the eyeball follows coagulation of both long posterior ciliary arteries (Guerry). In my first case, the eye in which, in two stages, both the upper and the lower half were treated seems to be tending toward atrophy, the tension being 9 mm. four months after operation. On the other hand, one-half the circumference of the other eye was treated and the tension is 60 mm. of mercury, but there is no pain. There was also slight atrophy in the case reported by Scobee. I do not know the late results obtained by Meyer and Sternberg, but these authors emphasize the pain-relieving action of the procedure. All this evidence together shows that cyclodiathermy done in a case of rubeosis iridis seems to lead easily to atrophy of the eyeball. Organization of the hemorrhage into the vitreous, so frequent during this disease, is probably a contributing factor. At first not more than one-half the ciliary body should be treated, care being taken to avoid the area of one of the two long posterior ciliary arteries. If the tension or the pain persists, another quadrant can be worked on, the remaining posterior ciliary artery being spared.

I shall not discuss here the pathogenesis of diabetic rubeosis iridis. I wish to mention only one point, namely, that the damaged kidney seems to be a predisposing factor. Among the first changes in the eye due to diabetes are the enlargement and other alterations of the retinal veins. Does the presence of a renal lesion facilitate the accumulation of substances producing the vascular damage?

1a. Since this paper was written, a third case of the same condition has been observed in the blind right eye of M. M., a man aged 62, who had had diabetes for twenty years. Cyclodiathermy was performed on June 5, 1945 for pain and tension of 65 mm. with the same technic as that employed in case 1. On November 6 the tension was 12 mm., and the patient has been free from pain since the operation.

2. Vogt, A.: Cyclodiathermy Puncture in Cases of Glaucoma, Brit. J. Ophth. **24**:288, 1940.

3. Albaugh, C. H., and Dunphy, E. B.: Cyclodiathermy, Arch. Ophth. **27**:543 (March) 1942.

4. Meyer, S. J., and Sternberg, P.: Surgical Management of Glaucoma in Correlation with Gonioscopy and Biomicroscopy, Tr. Am. Acad. Ophth. (1944) **49**: 147, 1945.

5. Scobee, R. G.: Rubeosis Iridis Diabetica, Texas State J. Med. **40**:432, 1944.

6. Guerry, D., III: Angiodiathermy in Treatment of Glaucoma, Am. J. Ophth. **27**:1376, 1944.

In conclusion, it can be stated that after disappointing results with various types of operations, cyclodiathermy is the only procedure thus far found to lower the tension in cases of glaucoma due to rubeosis iridis diabetica. However, the treatment easily results in atrophy of the eyeball if used too extensively, particularly if both long posterior ciliary arteries are destroyed. These vessels should not be damaged if the rule laid down by Vogt is followed, i. e., if the applications are made in front of the insertion of the rectus muscles. But even if the cyclodiathermy is not done over a sufficiently large area to normalize the tension, it does alleviate the pain. Unfortunately, the progression of the damage to the retinal vessels cannot be checked.

Old National Bank Building.

OCULOMOTOR PARALYSIS WITH PARTIAL RECOVERY

REPORT OF A CASE

MAX CHAMLIN, M.D.
NEW YORK

Lesions of the third, fourth and sixth cranial nerves are always of interest to the neurologist and the ophthalmologist. Lesions of the third nerve, particularly, attract a great deal of attention because of the widespread distribution of this nerve. The present case is one of paralysis of the third nerve with internal and external ophthalmoplegia in which abnormal reactions to drugs were exhibited. The patient was observed over a long period, during which there was partial recovery with corresponding changes in the drug reactions and the appearance of the pseudo-Graefe phenomenon.

A white woman aged 68 was first observed at the Montefiore Hospital in January 1944. The history of her symptoms dated back to May 1943, at which time she complained of the sudden onset of pain in the left side of the head followed by gradual closing of the left eye in the next six days. Soon after the onset she was admitted to a large hospital, where the clinical picture was that of complete paralysis of the third nerve probably due to cerebral aneurysm.

The rest of her history disclosed no facts relevant to this condition. General examination revealed no evidence of syphilis, either clinical or serologic, and the blood chemistry was normal. The patient was found to have complete ptosis of the left upper lid (fig. 1 *A*). Voluntary effort to raise the lid resulted only in a slight upward pull of the skin, and even this could easily be eliminated by pressing a finger firmly against the supraorbital ridge, thus showing that the elevation of the skin was due to action of the frontalis muscle. Even with the aid of the frontalis muscle, however, no palpebral aperture was seen. When the lid was raised for the patient, the eye was found to be deviated outward and slightly downward (fig. 1 *B*). The left pupil was dilated to 4.5 mm., as compared with 2.5 mm. on the right side (fig. 1 *B*).

All the ocular muscles innervated by the third nerve were found to be paralyzed. On the patient's attempting to look to the right, the right eye rotated outward, while the left globe followed slowly as far as the midline and then stopped. This was evidently due to relaxation of the external rectus muscle alone. From this position, on her attempting to look down and to the right, the nasal pericorneal vessels along the horizontal meridian were seen to be carried downward, thus indicating intorsion of the left globe by the left superior oblique muscle. Therefore, the lateral rectus and the superior oblique were the only external muscles of the left eye that were functioning.

The left pupil did not react to light, either directly or consensually. A light thrown into the left eye, however, resulted in contraction of the right pupil.

Accommodation was tested, but the results were not conclusive. Of course, at the age of 68 there is so little accommodation that measurements are not satisfactory.

At the time I first saw the patient the neurologists made a diagnosis of cerebral aneurysm. Since the paralysis of the third nerve was so complete, it is quite unlikely that the nucleus proper was involved, because any lesion extensive enough to include every part of the nucleus of the third nerve on one side would, in all likelihood, involve the fourth nerve on that side and/or some portion of the nucleus of the contralateral third nerve. Therefore, it was probably the nerve trunk proper which was involved somewhere at the base of the brain.

Fig. 1.—*A* (January 1944) complete ptosis of the left eye; *B* (January 1944), deviation of left eye down and out and dilatation of left pupil; *C* (July 1944), partial recovery of ptosis on the left side.

To localize an aneurysm exactly in the neighborhood of the third nerve trunk at the circle of Willis is, at best, difficult. According to Dandy,[1] the diagnosis of an intracranial aneurysm can be made and its exact location ascertained only by one of three methods: necropsy, operation or angiographic examination. Dandy found paralysis of the third nerve in 30 per cent of his cases of intracranial aneurysm.

From the Ophthalmological Service of the Montefiore Hospital for Chronic Diseases.

Presented at a meeting of the New York Society for Clinical Ophthalmology, Dec. 4, 1944.

1. Dandy, W. E.: Intracranial Arterial Aneurysms, Ithaca, N. Y., Comstock Publishing Co., Inc., 1944, p. 23.

In Dandy's tables of reported cases,[2] the present case seems to fall most nearly among those of aneurysms of the internal carotid artery just after it has entered the cranial cavity, on its posterior aspect and in the neighborhood of the posterior cerebral arteries. It is in this particular area that the third nerve trunk is most likely to be implicated without inclusion of the fourth and sixth cranial nerves. Dandy reported 17 cases of partial or complete involvement of the third nerve by aneurysms in this area. The average age of the 17 patients was 41 years, as compared with this patient's age of 68. In any event, because of the complete paralysis of the third nerve and the absence of involvement of the other cranial nerves, it was thought that this patient's aneurysm was located in the internal carotid artery just after it enters the cranial cavity, in the region of the posterior cerebral vessels.

Since there was internal as well as external ophthalmoplegia, an investigation was made of the reactions of the paretic sphincter and ciliary muscles to drugs. Because the innervation of the sphincter and ciliary muscles is dependent on the cholinergic system, in the case of the muscles through the third nerve, mydriatics and miotics affecting the cholinergic and adrenergic systems were used.

Pilocarpine nitrate, 2 per cent, when instilled in both eyes contracted the right pupil from 2.5 to 1.5 mm. and the left pupil from 4.5 to 2.5 mm. (fig. 2). However, 1 per cent physostigmine salicylate, when instilled in both eyes, contracted the right pupil to 1.5 mm., but the left pupil remained unchanged, at 4.5 mm. (fig. 2).

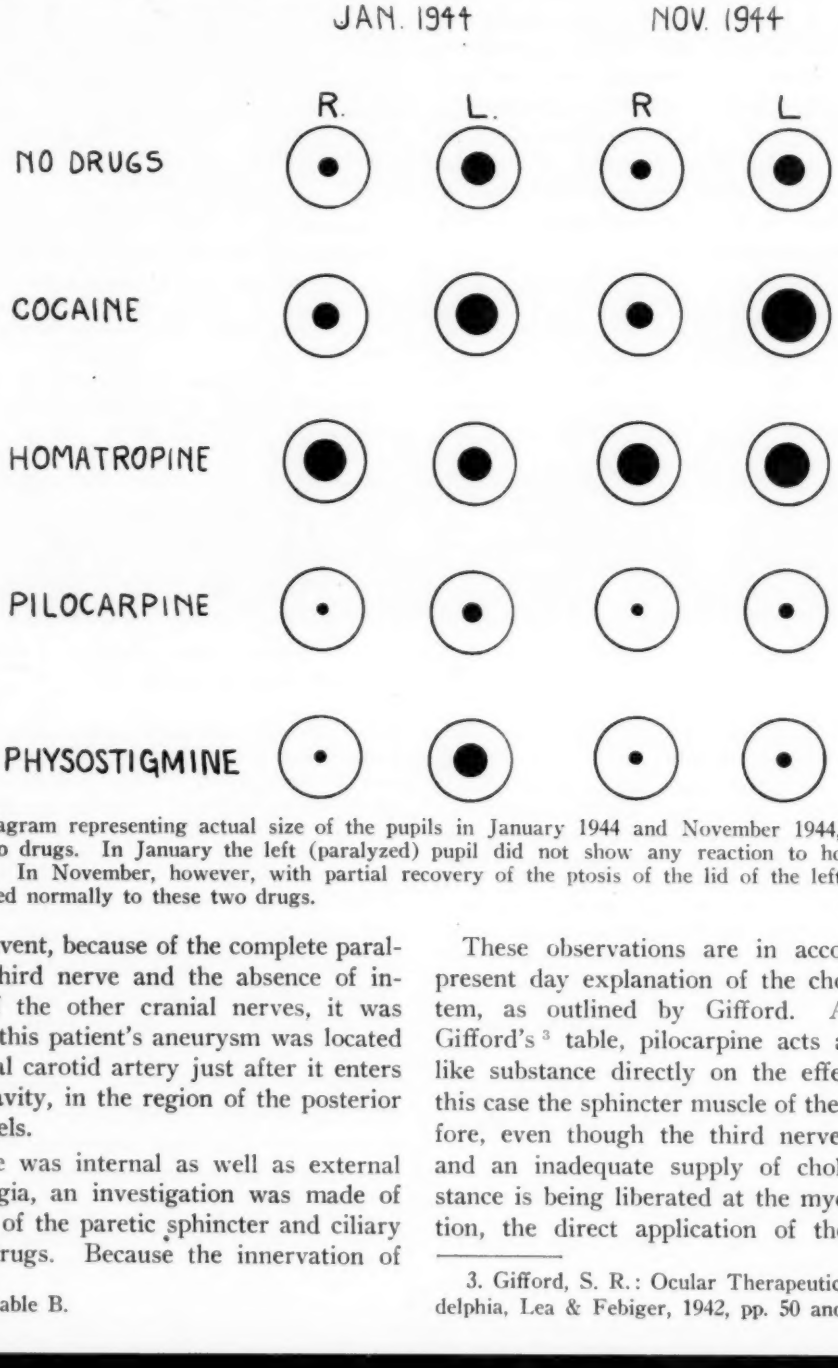


Fig. 2.—Diagram representing actual size of the pupils in January 1944 and November 1944, together with the reactions to drugs. In January the left (paralyzed) pupil did not show any reaction to homatropine and physostigmine. In November, however, with partial recovery of the ptosis of the lid of the left (paretic) eye, the pupil reacted normally to these two drugs.

These observations are in accord with the present day explanation of the cholinergic system, as outlined by Gifford. According to Gifford's [3] table, pilocarpine acts as a choline like substance directly on the effector unit, in this case the sphincter muscle of the iris. Therefore, even though the third nerve is defective and an inadequate supply of choline-like substance is being liberated at the myoneural junction, the direct application of the pilocarpine

2. Dandy,[1] table B.

3. Gifford, S. R.: Ocular Therapeutics, ed. 3, Philadelphia, Lea & Febiger, 1942, pp. 50 and 55.

replaces the acetylcholine and the sphincter muscle contracts. On the other hand, physostigmine acts by neutralizing the cholinesterase, which is constantly present at the myoneural junction and keeps the choline-like substance produced in check. With lesions of the third nerve, however, one may assume that choline-like substance is not being produced in sufficient quantity at the myoneural junction and that therefore, even though the cholinesterase is being neutralized by physostigmine, there is not enough acetylcholine produced by the defective third nerve to cause miosis. Thus, one can logically explain the absence of a miotic effect of physostigmine in this case. This action of physostigmine in causing acetylcholine to be made available is well known in physiology, and the experimental demonstration has been corroborated by clinical studies before.[4]

As adrenergic drugs, I used cocaine and homatropine. Cocaine dilated the right pupil from 2.5 to 3.5 mm. and the left pupil from 4.5 to 5.5 mm. (fig. 2). When, however, homatropine was instilled into the eyes, the right pupil dilated to 5.5 mm. but the left pupil remained at 4.5 mm. Here, again, my results are in accord with the action of the adrenergic system, as presented by Gifford.[3] Cocaine sensitizes the smooth muscle in the dilator of the iris to the ever present sympathin E at the myoneural junction. Its action is in no way dependent on the production of acetylcholine and therefore the mydriasis with cocaine takes place. Homatropine, however, acts by preventing the action of choline-like substance on the sphincter of the iris, thus allowing sympathetic tone to dominate and thereby causing mydriasis. Here, again, since the innervation of the third nerve is defective, one may assume that acetylcholine present is insufficient in amount to be influenced by the homatropine and that, therefore, there is no dilation by the homatropine.

Thus there is an internal and an external ophthalmoplegia.

The patient was observed at intervals and showed no change in her clinical appearance until July 1944, fourteen months after the onset of her symptoms. At this time the ptosis began to diminish, the width of the palpebral fissure of the left eye measuring 3.5 mm., as compared with 8.5 mm. on the right side (fig. 1 *C*). The four extraocular muscles innervated by the third nerve were still paretic. The pupil was still dilated and did not react to light (fig. 2). However, when both eyes were reexamined with the miotics and mydriatics, unlike the responses in January, the reactions of the left eye to drugs were now normal; i. e., physostigmine produced miosis and homatropine mydriasis (fig. 2). The persistent absence of the reaction to light may be attributed to the lack of sufficient acetylcholine for this reaction. Lowenstein and Givner,[4] in their study of a case of cyclic oculomotor paralysis, described clinically the acetylcholine requirement of the iris for reaction of the sphincter to light. The same investigators found that when the amount of available acetylcholine was not quite enough for the reaction to light to take place, the instillation of physostigmine would make more acetylcholine available and thus help to produce the response.

With the administration of the various drugs, a study of the intraocular tension was made. Prior to the instillation of drugs the tension in the two eyes was normal and equal on all occasions. After the administration of drugs various changes were found. While these changes were not sufficiently pronounced or constant to make possible definite deductions, the reactions of the paretic eye resembled somewhat those of a glaucomatous eye. For example, in May 1944, when the pharmacologic reaction of the left eye was beginning to return to normal, both pupils contracted twenty-one minutes after the instillation of physostigmine in both eyes, but, whereas the intraocular tension in the normal eye increased from 19 to 21 mm. of mercury, the tension in the paretic eye decreased from 19 to 16 mm. of mercury. This test was repeated in June 1944. Eighteen minutes after the administration of physostigmine, tension in the normal eye rose from 19 to 21 mm. of mercury, whereas the tension in the paretic eye fell from 19 to 14 mm. of mercury.

The increase in intraocular tension following instillation of physostigmine was described by Adler[5] as a normal phenomenon and is due to the dilatation and increased permeability of the capillaries to protein, with increased protein content of the aqueous and consequent rise in intraocular tension. On the other hand, with the contraction of the pupil of the paretic eye, the tension did not rise but actually fell. This is characteristic, rather, of the response of a glaucomatous eye. Therefore, although the paretic eye did not show any increased intraocular tension with the dilatation of the pupil, it did react to physostigmine like a glaucomatous eye, in contrast to the nonparetic eye, which reacted like any other normal eye.

4. Lowenstein, O., and Givner, I.: Cyclic Oculomotor Paralysis, Arch. Ophth. **28**:821 (Nov.) 1942.

5. Adler, F. H.: Clinical Physiology of the Eye, New York, The Macmillan Company, 1933, p. 375.

Adler suggested that physostigmine may not reduce tension in cases of acute glaucoma with increased intraocular pressure and dilated pupil because the tension causes paralysis of the third nerve; that is, the defect of the third nerve decreases the production of acetylcholine and, since the presence of acetylcholine is necessary for the action of the physostigmine to take place, the physostigmine alone may not contract the pupil in acute glaucoma. While it is not suggested that glaucoma is due to paralysis of the third nerve in any form, it is shown that both conditions may respond similarly to physostigmine with respect to the intraocular pressure.

A search of the literature for other cases of paralysis of the third nerve associated with features of glaucoma revealed a case described by Smith,[6] in which after trauma, with parasympathetic paralysis, a rise in intraocular tension was observed. If one concedes that glaucoma and paralysis of the third nerve may have common features, the next question is that of cause and effect. Thus, dilatation due to paralysis of the third nerve may produce a picture resembling glaucoma, whereas a rise in intraocular pressure may cause paralysis of the intraocular branches of the third nerve. The full explanation undoubtedly awaits much more experimental work.

Another interesting sign in the present case, noted in July 1944, fourteen months after onset of symptoms, was the "pseudo-Graefe" phenomenon, as described by the late Dr. Bielschowsky.[7] This phenomenon has been described in the stage of recovery of paralysis of the third nerve. When the patient looks down and to the nonparetic side, the upper lid of the paretic eye, instead of following downward or remaining ptosed, actually is elevated and even retracted, thus giving the impression of the Graefe sign, as seen with the exophthalmos of thyrotoxicosis (fig. 3 *A*). With this retraction of the upper lid, Bielschowsky described miosis of the paretic pupil. In the present case no miosis was observed.

According to Bielschowsky,[7] the "Graefe phenomenon" was explained by Fuchs as follows: Because the third nerve is atrophic, an impulse intended for one muscle is likely to spread to others as well. Bielschowsky, however, expressed the belief that the phenomenon is more probably due to an actual regrowth of fibers in the process of healing, so that the new fibers wander from the main trunk and grow into the wrong peripheral sheaths. Dandy cited Fox and Woodhall, who demonstrated this misdirection of fibers.[8] Thus, an impulse intended for one muscle will stimulate another. Bielschowsky stated the belief that these misdirected fibers tend to follow definite paths in growing into the wrong sheaths, so that "in the majority of cases, the impulse to look down and in produces the strongest contraction of the levator of the upper lid." One should note, however, that he used the term "in the majority of cases." He explained this point, showing that even when the patient attempts internal rotation of the eye without trying to look down, one can produce this retraction of the lid.

In the case presented here, besides exhibiting retraction of the upper lid on attempting to look down and *IN*, which is the classic picture, the patient also showed some elevation of the upper lid on attempting to look down and *OUT* (fig. 3 *B*). While the retraction in this case was not so pronounced as in the classic picture (fig. 3 *B*), it was still a definite elevation, whereas normally,

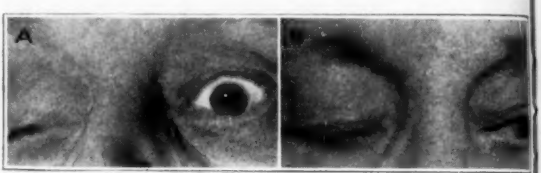


Fig. 3.—*A* (July 1944), "pseudo-Graefe" phenomenon. The patient is attempting to look down and to the right, with the right (normal) eye in that position. With the attempt to turn the paretic (left) eye down and in, the paretic lid, instead of being lowered, actually undergoes marked retraction. *B* (July 1944), patient attempting to look down and to the left, with the right (normal) eye in that position. With the attempt to turn the left (paretic) eye out and down, the paretic lid is raised.

on the subject's attempting to look down and *OUT*, the lid would move down with the globe. Some elevation or retraction of the left upper lid was produced in directions of gaze other than the two just mentioned.

SUMMARY

A case of internal and external ophthalmoplegia due to paralysis of the third nerve is described.

Because of the internal ophthalmoplegia, an opportunity was afforded to study the effects of various drugs on the paretic pupil during the

6. Smith, H. J.: Am. J. Ophth. **25**:211 (Feb.) 1942.

7. Bielschowsky, A.: Lectures on Motor Anomalies, Hanover, N. H., Dartmouth College Publications, pp. 83 and 84.

8. Dandy,[1] pp. 11 and 12.

paretic stage as well as during partial recovery. The reactions observed fit well into the present day concept of the mode of action of the cholinergic and adrenergic drugs.

Since the light reflex had not returned at the time that the normal pupillary reactions to homatropine and physostigmine did, one may assume that a stronger cholinergic tone is necessary for the light reflex than that required to produce reactions to these two drugs.

While there was no increase in intraocular tension, the reaction to physostigmine resembles that of a glaucomatous eye.

The "pseudo-Graefe" phenomenon seen in the stage of recovery of paralysis of the third nerve is illustrated. This retraction of the paretic lid can be produced by having the patient attempt to look in directions other than the classic "down and in."

1840 Grand Concourse.

CONGENITAL RETINAL FOLD

CAPTAIN EMANUEL ROSEN
MEDICAL CORPS, ARMY OF THE UNITED STATES

Congenital retinal fold has been reported so infrequently and on such occasions has been explained so incompletely, with so much room for questioning, that any report of a case which might suggest one further point in its development would seem to be welcome. The cases reported of this condition are so few that the presentation of almost any new case should add some new feature, or at least lead to discussion or modification of the present concept of the anomaly. After a review of some of the cases in the literature a few variations seem to present themselves in the 2 cases reported here. Subsequent study might be directed particularly along such lines.

Pathologic material was obtained in many of the early cases, since the eye was enucleated for supposed glioma and only on histologic study was the true nature of the "pseudoglioma" worked out. The name "congenital falciform ligament" was taken from the "falciform process" found in the teleostean eye, which this anomaly resembles and the resemblance to which caused Mann to suggest that the condition was of atavistic significance.

REPORT OF CASES

CASE 1.—A 26 year old man stated that he had been unaware of the poor vision in his left eye until he was 11 years old, at which time he was involved in an automobile accident. After the accident his vision was tested and found to be poor. The accident did not require hospitalization, and there was no serious head trauma. The patient continued to believe that the poor vision in the left eye was the direct result of this trauma, for he had not been told otherwise. In the ensuing years he did not notice any change in this eye; there was at no time any indication of an inflammatory process developing in the eye.

All members of his family, which included his parents, 2 brothers and 2 sisters, wore glasses, but no one had vision which could not be improved with glasses. The family history was negative for congenital anomalies, as well as for all types of apparent ocular disorders.

When the patient's mother was five months pregnant, she had a severe attack of measles, during which she remained in bed for two weeks. The attack was a serious one; in her own words, "The measles settled in my head, and it was three months before I could hear again. I had a head specialist during this time to treat my head. I can't quite remember how high my fever was, but I know it was 102 or 103 [F.] for quite some time." She also stated that until he was 16 years old she had been unaware of her son's inability to see out of one eye.

The patient also had impairment of hearing in his left ear of many years' duration, which he believed to be nonprogressive. There were no other physical defects of any significance.

The fundus of the left eye showed the unusual picture illustrated in figure 1. The main feature was the large white, falciform mass stretching from the upper to the lower portion of the retina in the 1 to 7 o'clock axis. This mass was well anterior to the retina but stretched back to form an attachment with the retina except at its free ends. It overhung the disk, so that only a small portion of that structure could be seen unless an attempt was made to look around the fold. In this case the disk appeared to have a rather sharp anterior edge except at its lower extremity, where it rotated, becoming somewhat shelved, and then frayed out into multiple dentate processes, which blended indistinctly into the vitreous. The superior portion of the fold was nodular and clubbed. Its termination also suggested an imperceptible blending into the vitreous. The fold was grayish white and seemed to be striated much as the retina appears when medullated. There were no grooves in the fold and no signs of any patencies or foramens as the nerve head was approached. The entire fold was avascular. The light from the ophthalmoscope threw a shadow along either side of the falciform ligament. There was no attachment of the fold to any portion of the lens. The fold had a slightly sinuous arrangement.

The disk, which could be seen only partially, was pinkish yellow and approximately three times the normal size of the disk. Arranged somewhat obliquely, it gave the appearance of having been drawn out irregularly by traction of the congenital retinal fold. Its margins were scalloped but not indistinct. The pattern of the blood vessels emerging from the disk was atypical and nondescript. Some of the vessels coursed along the lateral walls of the congenital fold. In general the vessels were anomalous in size and distribution, so that in many places the artery could not be distinguished from the vein. The over-all pattern of the blood vessels tended toward a paucity of vascularization throughout the fundus, which feature has been pointed out as a characteristic of the condition.[1] At no place along the retinal fold did a vessel cross its sharp edge. A small round, white lesion, about the size of the disk, was present just below the macula. This lesion was horizontally oval and had a densely pigmented crescent bordering its upper edge. Many vessels, both large and small, coursed through it. One large vessel, passing inferiorly and nasally, had a pronounced parallel sheathing. Just above and slightly nasal to this lesion was a small crystalline, yellowish

1. Gartner, S.: Congenital Retinal Folds and Microcephaly, Arch. Ophth. **25**:93 (Jan.) 1941.

lesion with pigment granules within its center. The retina in general had a slightly atrophic appearance with many areas of dense pigmentation, together with regions where a peculiar sheen was prominent. Physical examination was noncontributory except that a decided tilt of the head to the left could not escape notice. There were no abnormalities of the heart, lungs, extremities or abdomen. Examination of the eyes showed nothing unusual except for the fundus of the left eye. The muscles, pupil, iris and lenses showed no abnormalities in either eye.

Case 2.—J. G., aged 17, was first seen at the ophthalmic clinic on Jan. 10, 1934, having come to the hospital primarily to seek aid for a pronounced convergent squint of the left eye. The patient stated that this eye had been turned in, with poor vision, all his life. He had worn glasses since the age of 4, although they seemed not to help his vision or his appearance.

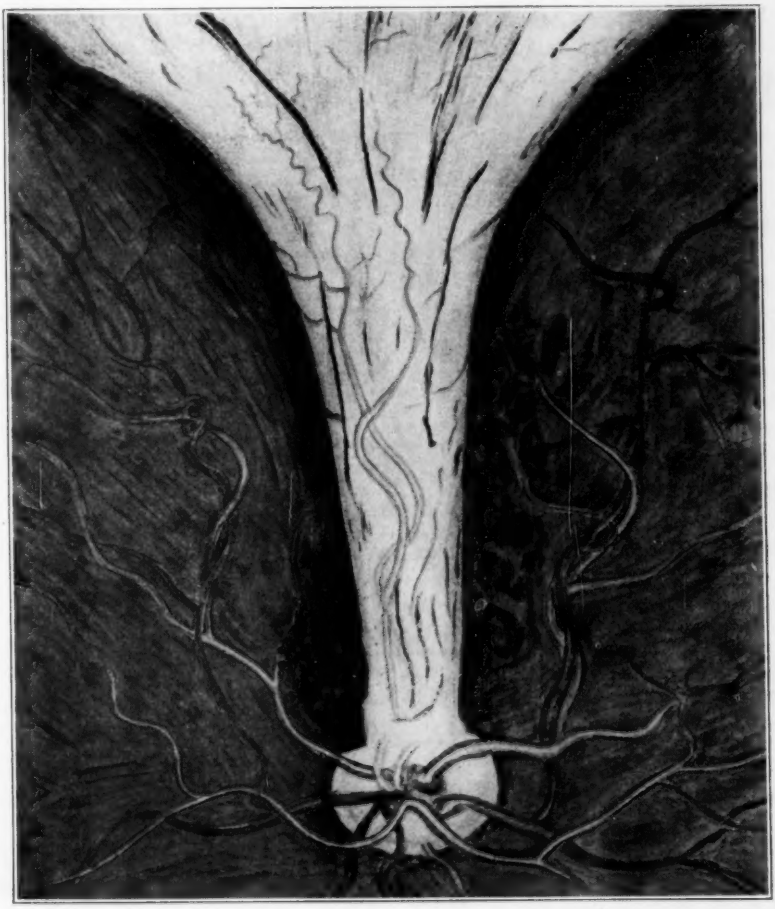


Fig. 1 (case 1).—Retinal fold extending on both sides of the optic disk, with a large macular lesion and obstructed vessel.

Vision was restricted to light perception in the left eye and was 20/20 in the other eye. The left eye had a marked "in-shoot," with a tendency to left hypertropia. On examination with the slit lamp, both eyes showed a fairly well developed persistent pupillary membrane. The right fundus was not unusual in any respect. The left fundus presented a large whitish gray, funnel-like mass, which began just temporal to the disk and extended to the postlental region, running almost horizontally and broadening out like a champagne glass from its stem (fig. 2). The mass, which was cylindric, seemed to draw the underlying retina to it in the form of a tent. Many old pigmented choroidal patches, dark brown and irregular in shape, were present on each side of the mass, and other pigmentary blotches were present in various parts of the tentorial elevation, pigment being much more pronounced in the area closest to the large funnel-like mass. Just beyond the temporal margin of the disk was an oblique cleft through which two large vessels passed; these vessels ran up the entire length of the mass and divided into many small twigs, some of which were unusually tortuous. A few twigs also ran up the under surface of the mass to terminate in some of the folds of that structure. In general, the vasculature of the fundus was not anomalous; neither was the disk or the physiologic cup strikingly unusual.

The white, funnel-like mass could not be followed to its most peripheral location, but no abnormality could be found in either lens. There were no other ocular abnormalities. The patient knew little about his parents and his brothers' eyes but believed there was nothing abnormal in any manner in these persons. Unfortunately, none of his kin were examined.

COMMENT

Congenital retinal fold is justifiably a reportable condition, for its existence has been recorded not much more than thirty times, the first report in the American literature appearing in 1940.[2] The majority of cases have been reported by Mann [3] and by Weve [4]—a total of 14 cases being listed by these authors. The series of cases analyzed by Mann were studied primarily from the embryologic and histologic points of view, since some of the patients were not seen clinically but only pathologic specimens were received, together with notations from the referring physicians. Weve's [4] studies, on the other hand, were conducted along clinical and genetic lines, with a careful consideration of familial factors. These two different avenues of approach explain in some manner the theoretic promulgations made by these authors; yet they are much alike.

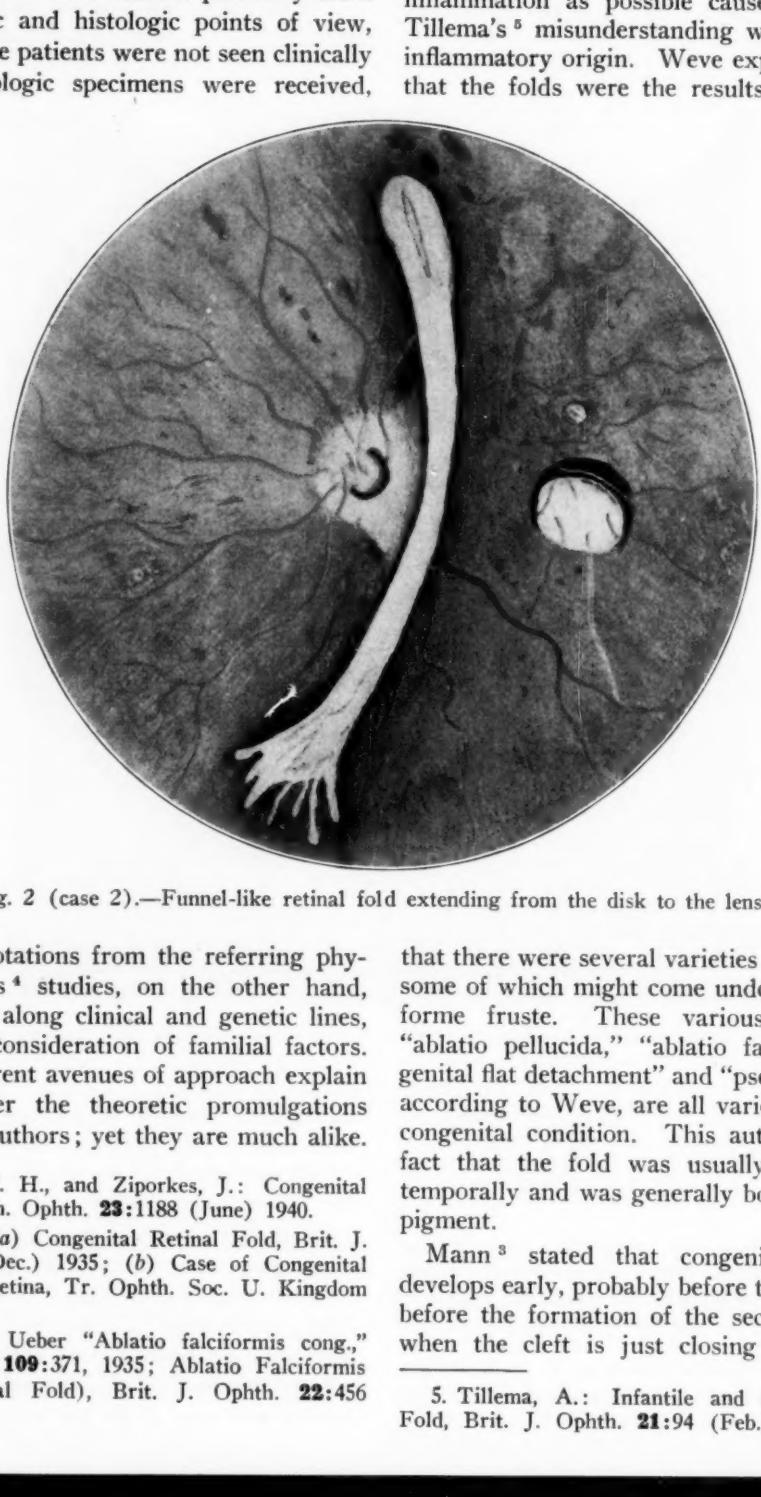


Fig. 2 (case 2).—Funnel-like retinal fold extending from the disk to the lens.

Weve's theory, viz., that these folds are formed by adhesions of the primary vitreous to the mesoderm of the anterior half of the eye, is essentially the same as Mann's theory of the adhesion of the primary vitreous to the inner margin of the optic cup. Weve placed emphasis on the fact that the central retainal fold was bilateral, symmetrical, familial and frequently associated with other congenital anomalies. He eliminated trauma and inflammation as possible causes and corrected Tillema's [5] misunderstanding with regard to an inflammatory origin. Weve expressed the belief that the folds were the results of traction and that there were several varieties of this condition, some of which might come under the heading of forme fruste. These various forms included "ablatio pellucida," "ablatio falciforme," "congenital flat detachment" and "pseudoglioma" and, according to Weve, are all varieties of the same congenital condition. This author stressed the fact that the fold was usually located inferotemporally and was generally bordered by heavy pigment.

Mann [3] stated that congenital retinal fold develops early, probably before the 13 mm. stage, before the formation of the secondary vitreous, when the cleft is just closing and the retinal

2. Theodore, F. H., and Ziporkes, J.: Congenital Retinal Fold, Arch. Ophth. **23**:1188 (June) 1940.

3. Mann, I.: (*a*) Congenital Retinal Fold, Brit. J. Ophth. **19**:641 (Dec.) 1935; (*b*) Case of Congenital Abnormality of Retina, Tr. Ophth. Soc. U. Kingdom **48**:383, 1928.

4. Weve, H.: Ueber "Ablatio falciformis cong.," Arch. f. Augenh. **109**:371, 1935; Ablatio Falciformis Congenita (Retinal Fold), Brit. J. Ophth. **22**:456 (Aug.) 1938.

5. Tillema, A.: Infantile and Congenital Retinal Fold, Brit. J. Ophth. **21**:94 (Feb.) 1937.

layers are still undifferentiated. The hyaloid system seems to hinder the formation of the secondary vitreous. In all of Mann's sections traces of the contents of the primary vitreous were adherent to the fold, and in all cases the fold involved the inner layer of the optic cup. In these case reports the solid appearance of the septum, the presence of branches of the retinal artery on the fold, the attachment anteriorly to the ora serrata and the passage of strands to the lens near the equator were pointed out as definite characteristics. In all cases strands of persistent embryonic vessels were supposedly adherent to the surface of the fold. From histologic studies Mann stated [3a]:

> It is quite evident that the condition is a double fold of retina pulled inwards and attached to an abnormally persistent hyaloid. The inner layer of the optic cup is alone involved in the fold, the pigment epithelium being unaffected. . . . In all cases . . . examined microscopically the whole of the retina shows imperfect differentiation. . . . We are dealing with a disturbance of growth of the whole of the inner layer of the optic cup at an early age.

The three main considerations emphasized by Mann from the embryologic standpoint were the nature of the tissue in the retinal fold, the relation of the retinal fold to the hyaloid artery and the position of the fold. She offered no explanation of the cause of vitreous adhesions. Although hemorrhage at an early stage could not be excluded, the bilateral, symmetric and hereditary nature of the condition in some of the cases seemed to rule out such a causative element.

The recent studies of Gregg [6] and Swan and associates,[7] showing the production of congenital cataract in infants whose mothers had contracted rubella in the early months of pregnancy, point to the increased susceptibility of embryonic tissues, particularly to virus infections. These authors stated the belief that susceptibility is fairly well limited to the first three months of pregnancy, at which time the virus penetrates the chorionic barrier with ease. After that period the placenta forms and acts as a barrier to the virus.[8] The mother of my patient (case 1) was about five months pregnant when she had measles, which "settled in her head"—she could not hear for three months. The patient apparently suffered from a virus disease during or close to the fifth month of pregnancy, which produced acute cephalalgic symptoms and which possibly was transmitted to the embryonic tissues, particularly the neuro-ophthalmologic elements.

Van Manen [9] suggested that the congenital retinal fold is a hyperplasia of the fetal neuroglia. He stated that this glial tissue reaches its maximum extent in the fifth fetal month, forming a system of funnel-shaped sheaths around the fetal hyaloid vessels, which afterward disappear. As the eye develops, this abnormally persisting tissue is tightened into a cordlike structure running through the eyeball by means of the centrally pushed primary vitreous. If a fetal adhesion exists between the hyaloid vessel and the inner layer of the retina, a tentlike fold will result. In van Manen's case report he attached considerable importance to this "cudgel-like" appearance and shape of the anomaly, particularly with respect to the groove near the disk, through which he stated the hyaloid vascular system runs. The retina was adherent to the posterior surface of the cudgel-like mass along its entire length and was lifted up from its pigment layer like a tent. Because the father of van Manen's patient had a congenital opacity of the lens, the author suggested that the same disturbance in the germ layer of the father and the son gave rise to two different congenital abnormalities of the eye, possibly the result of faulty nutrition of the lens through disturbance in the hyaloid system in the case of the father.

Theodore and Ziporkes [2] reported 4 cases of congenital retinal folds. In case 1 the congenital retinal fold ran on both sides of the disk; this is the only case besides the first one reported here in which this feature was shown. In case 1 of Theodore and Ziporkes there were several secondary folds. The mother of the patient in case 2 presented by these authors had congenital cataract, together with a persistent hyaloid artery; this associated anomaly adds importance from the hereditary aspect. These authors also suggested that the macula is usually poorly developed, as is the retinal blood vessel system, both features being strikingly prominent in their cases. Theodore and Ziporkes, after discussing the various theories, were inclined to accept the theory put forward by Ida Mann, although they could not completely disregard the familial and hereditary features pointed out by Weve. Mental deficiency was an occurrence in 2 cases, namely, in the first case reported by Guerry [10] and in Gartner's [1] case. In

6. Gregg, N. M.: Congenital Cataract Following German Measles in Mother, Tr. Ophth. Soc. Australia (1941) **3**:35, 1942.

7. Swan, C., and others: Congenital Defects in Infants Following Infectious Diseases During Pregnancy, M. J. Australia **2**:201 (Sept. 11) 1943.

8. Rados, A.: Epidemic Keratoconjunctivitis and Virus Diseases of Eye, Arch. Ophth. **32**:308 (Oct.) 1944.

9. Van Manen, J. G.: Congenital Anomaly of Fundus Oculi, Arch. Ophth. **26**:1 (July) 1941.

10. Guerry, DuP., III: Congenital Retinal Folds: Report of Two Cases, Am. J. Ophth. **27**:1132 (Oct., pt. 1) 1944.

Guerry's second case a congenital retinal fold was present in one eye and a congenital retinal detachment in the second eye, this being the only case on record in which these two conditions were found in different eyes of the same patient. Guerry stated that this case "lends weight to Weve's conjecture that congenital retinal folds are closely related to congenital retinal detachments."

It has been pointed out that when there is a bilateral congenital retinal fold it is usually symmetric in shape and position. When this is true, it would seem that the abnormality occurred very early in the embryonic development, possibly even before the 13 mm. stage, as emphasized by Mann. In the cases of a unilateral fold it is possible that the factor responsible for maldevelopment does not involve that portion of the susceptible retina or vitreous until a much later date. When the fold is unilateral, it is very likely to be taken for "glioma," since emphasis has been placed on bilaterality in the congenital condition, although this condition does not necessarily appear to be characteristic.

Both Gartner and Theodore and Ziporkes have emphasized the character of the blood vessels, pointing out several features which were pronounced in 1 of the cases reported here. These features include the anomalous size and distribution of the blood vessels, the general paucity of blood vessels throughout the fundus, the prominent attenuation of the vessels and the difficulty in differentiating the veins from the arteries. Gartner also noted the glazed, atrophic and pigmentary disturbance of the retina, which description applies adequately to our case 1. The surface of the retinal fold is supposedly grayish but becomes somewhat pink as the disk is approached. Such changes in the retina probably result from inadequacy of blood supply, which in some manner is disturbed by the abnormal fold and the abnormal hyaloid circulation. The nature of the retina in these cases may be a clue to the time of formation of the fold and, again, may explain the secondary anatomic differences in the various cases.

INTRAOCULAR PENETRATION OF STREPTOMYCIN FOLLOWING SYSTEMIC AND LOCAL ADMINISTRATION

IRVING H. LEOPOLD, M.D., D.Sc.
AND
ANNE NICHOLS, M.S.
PHILADELPHIA

Waksman and his associates have isolated two apparently related substances, streptothricin [1] and streptomycin, [2] from the genus Streptomyces which are more bacteriostatic or bactericidal for gram-negative bacilli than is penicillin. Of the two, streptomycin has been shown to be less toxic and to possess greater action against certain gram-negative and gram-positive bacteria in vivo [3]. Streptomycin has been demonstrated to be beneficial in treatment of experimental infections due to Proteus vulgaris [4], Pasteurella tularenis,[5] Mycobacterium tuberculosis [6] and organisms of the Friedländer group [7] in animals. Recently streptomycin was shown to have possible benefit in cases of typhoid infection in man.[8]

Zintel and his co-workers [9] have shown that the concentration of streptomycin in the blood following a single intravenous injection is better maintained than that of penicillin. Detectable amounts were usually present six hours after intramuscular administration, as compared with two to three hours in the case of penicillin. Early side reactions were not alarming, and the authors observed no late toxic effects from systemic administration.

Because of the possibility of streptomycin being of value for ocular infections, it seemed advisable to determine the intraocular penetration of this compound with various modes of administration.

METHODS OF INVESTIGATION

Modes of Administration.—The following modes of systemic administration of streptomycin were studied experimentally: (1) intravenous injection of 10,000 units per kilogram, (2) intramuscular injection of 10,000 units per kilogram, (3) intravenous injection of 100,000 units per kilogram and (4) intramuscular injection of 100,000 units per kilogram, of body weight.

The following modes of local administration of streptomycin were studied experimentally:

1. Instillation of 5 drops of a solution of streptomycin containing 5,000 units per cubic centimeter of isotonic solution of sodium chloride. Each drop was instilled at an interval of thirty seconds.

2. Instillation of 0.1 Gm. of an ointment containing 5,000 units of streptomycin per gram of ointment base. The ointment base was a polyethylene glycol (Carbowax) and propylene glycol in equal proportion, as previously used for penicillin.[10]

The streptomycin used in this study was supplied by Merck & Co., Inc., through the Committee on Medical Research.

From the Department of Ophthalmology and the Harrison Department of Surgical Research of the University of Pennsylvania School of Medicine.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania.

1. Waksman, S. A., and Woodruff, H. B.: Streptothricin—A New Selective Bacteriostatic and Bactericidal Agent, Particularly Active Against Gram-Negative Bacteria, Proc. Soc. Exper. Biol. & Med. **49**:207-210, 1942.

2. Waksman, S. A.: Production and Activity of Streptomycin, J. Bact. **46**:299-310, 1943. Schatz, A.; Bugie, E., and Waksman, S. A.: Streptomycin: A Substance Exhibiting Antibiotic Activity Against Gram-Positive and Gram-Negative Bacteria, Proc. Soc. Exper. Biol. & Med. **55**:66-29, 1944.

3. Robinson, H. J.; Smith, D. H., and Graessle, O. E.: Chemotherapeutic Properties of Streptomycin, Proc. Soc. Exper. Biol. & Med. **57**:226-231, 1944.

4. Waksman, S. A.; Bugie, E., and Shatz, A.: Isolation of Antibiotic Substances from Soil Micro-Organisms, with Special Reference to Streptothricin and Streptomycin, Proc. Staff Meet., Mayo Clin. **19**:537-548, 1944.

5. Heilman, F. R.: Streptomycin in the Treatment of Experimental Tularemia, Proc. Staff Meet., Mayo Clin. **19**:553-559, 1944.

6. Feldman, W. H., and Hinshaw, H. C.: Effects of Streptomycin on Experimental Tuberculosis in Guinea Pigs, Proc. Staff Meet., Mayo Clin. **19**:593-599, 1944.

7. Heilman, F. R.: Streptomycin in the Treatment of Experimental Infection with Micro-Organisms of the Friedländer Group (Klebsiella), Proc. Staff Meet., Mayo Clin. **20**:30-39, 1945.

8. Reimann, H. A.; Elias, W. F., and Price, A. H.: Streptomycin for Typhoid, J. A. M. A. **128**:175-180 (May 19), 1945.

9. Zintel, H. A.; Flippin, H. F.; Nichols, A. C.; Wiley, M. N., and Rhoads, J. E.: Studies on Streptomycin in Man: Absorption, Distribution, Excretion, and Toxicity, Am. J. M. Sc. **210**:421-430 (Oct.) 1945.

10. Leopold, I. H., and LaMotte, W. O., Jr.: Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, Arch. Ophth. **33**:43-46 (Jan.) 1945.

3. Instillation of drops of a solution of streptomycin containing 50,000 units per cubic centimeter of isotonic solution of sodium chloride.

4. Iontophoresis with a solution of streptomycin containing 5,000 units per cubic centimeter of isotonic solution of sodium chloride. A current of 2 milliamperes was maintained for three minutes. Special glass electrodes were used, as devised by von Sallmann.[11] The negative pole was applied to the eye electrode.

In all animal experiments, rabbits of a blue-eyed or brown-eyed chinchilla strain, weighing between 2.5 to 4 Kg., were used. Samples of aqueous humor to be analyzed for streptomycin content were obtained by making a limbal puncture with a sterile 26 gage hypodermic needle and a sterile tuberculin syringe. All eyes were topically anesthetized with 2 drops of 0.5 per cent tetracaine hydrochloride a few moments before the puncture was made. In all eyes that received streptomycin locally, the cul-de-sacs were thoroughly washed with sterile isotonic solution of sodium chloride before instilling the local anesthetic.

To obtain specimens of vitreous humor the eyes were enucleated and washed with sterile isotonic solution of sodium chloride; the sclera and the chorioretinal layers were incised with a sterile Bard-Parker knife, and the vitreous was drawn into a sterile pipet.

Specimens of secondary aqueous were obtained by reentering the anterior chambers of eyes previously used for specimens of primary aqueous humor.

Normal eyes were removed from 4 rabbits thirty minutes, two hours, four hours and six hours, respectively, after a single intramuscular injection of 10,000 units of streptomycin per kilogram of body weight. The eyes were enucleated while the animals were under ether anesthesia. These animals were then killed with intravenous injections of air. The following tissues of these eyes were analyzed for their streptomycin content: conjunctiva, extraocular muscles, cornea, lens, vitreous, chorioretinal layers, sclera and optic nerve. There were two eyes for each time interval. The time intervals at which these tissues were tested were thirty, one hundred and twenty, two hundred and forty and three hundred and sixty minutes after administration of streptomycin. All tissues were removed with sterile technic, weighed, transferred to a mortar and ground with sand, and a measured quantity of isotonic solution of sodium chloride added. After extraction each specimen was analyzed for streptomycin content. The same procedure was repeated using intramuscular injections of 100,000 units of streptomycin per kilogram of body weight. The time intervals for the second group were thirty minutes, two hours and four hours.

All the rabbit eyes were normal except for one group in which the corneas were experimentally abraded. The epithelium was removed from these corneas by rubbing the surface with gauze. Staining with fluorescein served as a guide to the extent of denudation. Approximately one fourth of each cornea was so denuded. Six hours was allowed to elapse after producing the denudations before such eyes were used for studies of penetration.

Method of Assay.—The cup method of assay was used.[12] Staphylococcus aureus strain SM was grown from four to six hours in Federal Drug Administration[13] broth p_H 6.8. The growth was diluted to 1:10,000 with broth. Ten cubic centimeters of this dilution was added to 90 cc. of previously melted and cooled Federal Drug Administration agar of p_H 7.5, containing 2.5 per cent sodium chloride. Ten cubic centimeters of the inoculated agar was added to each Petri plate by means of a sterile wide mouth pipet. Steel-beveled assay cups, 1 cm. in height and 8 mm. in diameter, were used. Two assay cups were placed on each agar plate. The cups were filled to the top with the standard streptomycin or tissue extract. The diffusion took place overnight in the ice box, after which the plates were incubated at 37 C. for eighteen to twenty-four hours.

The diameter of the zone of inhibition was measured in millimeters with the aid of a magnifying glass. A standard curve of streptomycin in distilled water was used to determine the concentration of streptomycin present in primary aqueous humor and in vitreous humor and in extracts of the lens and cornea. For secondary aqueous humor and all other tissue extracts a standard curve of streptomycin in normal human or rabbit serum was used. Dilutions of 1, 2, 4, 8, 10, 15, 20, 30 and 40 units of streptomycin were used for construction of the standard curve. The diameter of the zone of inhibition was plotted against the concentration of streptomycin as abscissa. An extract of each tissue was prepared by grinding it in 0.5 cc. of distilled water in a sterile mortar. Two or more cups were set up for each extract.

TABLE 1.—*Concentration of Streptomycin in the Aqueous Humor of Normal Rabbit Eyes Following Intravenous and Intramuscular Administration*

Time After Administration of Streptomycin, Min.	10,000 Units per Kilogram		100,000 Units Per Kilogram
	Intravenous, Units/Cc.	Intramuscular, Units/Cc.	Intravenously, Units/Cc.
5	1	0	
15	1	0	
30	2	0	35
60	1	1	30
120	2	8	21
180	1	6	20
240	3	4	
300	1	4	

RESULTS

In table 1 are listed the concentrations of streptomycin in primary aqueous humor of normal rabbit eyes following a single intravenous or intramuscular injection of streptomycin. When the amount injected amounted to 10,000 units per kilogram of body weight, comparable to a single intravenous injection of 600,000

11. von Sallmann, L.: Personal communication to the authors.

12. Stebbins, R. B., and Robinson, H. J.: A Method for the Determination of Streptomycin in Body Fluids. Proc. Soc. Exper. Biol. & Med. **59**:255, 1945.

13. Ruehle, G. L. A., and Brewer, C. M.: United States Food and Drug Administration Methods of Testing Antiseptics and Disinfectants, Circular 198, United States Department of Agriculture, December, 1931.

units in the average adult, streptomycin could be detected in the primary aqueous humor. It appeared in the aqueous humor within five minutes after the intravenous injection and could still be detected five hours later.

When the intravenous dose was raised to 100,000 units per kilogram, the concentration of streptomycin in the primary aqueous humor increased notably.

TABLE 2.—*Concentration of Streptomycin in Secondary Aqueous Humor of Rabbit Eyes Following Systemic Administration of 10,000 Units per Kilogram of Body Weight*

Time of Withdrawal of Secondary Aqueous Humor After Administration of Streptomycin, Min.*	Intravenous,† Units/Cc.	Intramuscular,† Units/Cc.
65	20	13
120	10	12
180	6	8

* All specimens of primary aqueous humors were withdrawn five minutes after administration of streptomycin.

† Each level represents the average values for two eyes.

Intramuscular administration of 10,000 units of streptomycin per kilogram of body weight produced detectable concentrations of streptomycin in the aqueous humor sixty minutes after the injection. Streptomycin was still definitely present in the aqueous humor five hours after the intramuscular injection.

In table 2 is recorded the concentration of streptomycin in secondary aqueous humor. A single intravenous or intramuscular injection

TABLE 3.—*Concentration of Streptomycin in the Aqueous Humor of Human Eyes Following a Single Intravenous Administration of 600,000 units of Streptomycin*

Patient	Ocular Condition	Units of Streptomycin per Cc. of Primary Aqueous Humor Withdrawn 30 Min. After Intravenous Injection	Units of Streptomycin per Cc. of Secondary Aqueous Humor Withdrawn 3 Hr. After Initial Puncture of Anterior Chamber	Units of Streptomycin per Cc. of Blood at Time of Initial Puncture of Anterior Chamber
S. W.	Absolute glaucoma	3	19	75
M. G.	Normal	1	3*	75
J. G.	Absolute glaucoma	3	10†	40

* Specimen taken ninety minutes after initial puncture of anterior chamber.

† Specimen taken thirty minutes after initial puncture of anterior chamber.

of 10,000 units of streptomycin per kilogram of body weight produced high concentrations of streptomycin in the secondary aqueous humor. (Compare with values in table 1.)

In table 3 are listed the concentrations in the aqueous humor in 3 human eyes following a single intravenous administration of 600,000 units of streptomycin. Streptomycin was detectable in the primary aqueous humor thirty minutes after the intravenous injection and was increased in the secondary aqueous humor in each instance.

A single intravenous injection of 10,000 units per kilogram of body weight failed to produce detectable levels in the vitreous humor. A similar dose administered intramuscularly did produce detectable concentration in the vitreous humor two hours after the injection. By increasing the dose of streptomycin to 100,000 units per kilogram for intravenous injection, definite concentrations of streptomycin were noted in the vitreous humor. The data are listed in table 4.

A single intramuscular injection, 10,000 units of streptomycin per kilogram of body weight, produced measurable concentrations of streptomycin in the conjunctiva, extraocular muscles

TABLE 4.—*Concentration of Streptomycin in the Vitreous Humor of Normal Rabbit Eyes Following Intravenous and Intramuscular Administration*

Time After Administration of Streptomycin, Min.	10,000 Units per Kilogram		100,000 Units per Kilogram
	Intravenous, Units/Cc.	Intramuscular, Units/Cc.	Intravenous, Units/Cc.
5	0	0	1
15	0	0	3
30	0	0	2
60	0	0	1
120	0	1	
180	0	1	
240	0	3	0
300	0	1	4

and sclera within thirty minutes, and streptomycin was present in these tissues for almost four hours. A detectable level was found in the chorioretinal layers only at two hours after such a dose (table 5). When the intramuscular dose was increased to 100,000 units per kilogram, the amounts of streptomycin in the conjunctiva, extraocular muscles and sclera were greatly increased, and levels were also obtained in the specimens of the chorioretinal layers, optic nerve and cornea. The concentrations reached were greatest in the conjunctiva. The extraocular muscles, the sclera, the chorioretinal layers, the cornea and the optic nerve showed decreasing amounts of streptomycin, in the order given. None was found in the lens. The graph demonstrates the relative concentrations in the ocular tissues after a single intramuscular injection of streptomycin.

LOCAL ADMINISTRATION

From the results recorded in table 6 it is evident that local application of solutions con-

taining 5000 units of streptomycin per cubic centimeter of isotonic solution of sodium chloride or of an ointment containing 5,000 units per gram of base penetrated into the aqueous humor of rabbit eyes with normal corneas in barely detectable amounts. Increasing the concentration of the solution to 50,000 units per cubic centimeter failed to increase the rate or the quantity of penetration. However, in eyes with corneal abrasions, the solutions containing 5,000 units per cubic centimeter of isotonic solution of sodium chloride and the ointment containing 5,000 units per gram of base produced high concentrations of streptomycin in the aqueous humor. These concentrations were still higher after drop instillations of a solution containing 50,000 units per cubic centimeter.

Iontophoresis with a solution of streptomycin produced high concentrations of streptomycin in the aqueous humor. The analyses are recorded in table 7.

raising the systemic dose from 10,000 to 100,0 units per kilogram of body weight. Likewi the levels of streptomycin in the conjunctiv sclera and extraocular muscles were considerabl increased by using 100,000 units instead 10,000 units per kilogram. With the large dose, streptomycin was found in the cornea optic nerve and chorioretinal tissues of the nor mal eye but not in the lens.

Quite likely the intraocular penetration streptomycin will prove to be enhanced in eye with inflammation. This is suggested by th notably increased concentrations of streptomyci

TABLE 5.—*Concentration of Streptomycin in the Ocular Tissues of Rabbits Following a Single Intramuscula Injection of Streptomycin Consisting of 10,000 or 100,000 Units per Kilogram of Body Weight*

Tissue	30 Minutes After Injection		120 Minutes After Injection		240 Minutes After Injection		360 Minutes After Injection of 10,000 Units/Kg.
	10,000 Units/Kg., Units/Gm. Wet Weight	100,000 Units/Kg., Units/Gm. Wet Weight	10,000 Units/Kg., Units/Gm. Wet Weight	100,000 Units/Kg., Units/Gm. Wet Weight	10,000 Units/Kg., Units/Gm. Wet Weight	100,000 Units/Kg., Units/Gm. Wet Weight	Units/Gm. Wet Weigh
Conjunctiva	8	18	10	35	1	37	1
Extraocular muscles	2	1.5	8	30	1	40	1
Cornea	0	0	0	1	0	1	0
Lens	0	0	0	0	0	0	0
Chorioretinal layer	0	0	1	1	0	4	0
Sclera	4	3	1	28	1	28	0
Optic nerve	0	0	0	1	0	1	0

TABLE 6.—*Concentrations of Streptomycin in Aqueous Humor of Rabbit Eyes Following Local Instillation Streptomycin in Solution and Ointment Vehicles*

Time of Puncture of Anterior Chamber After Instillation of Streptomycin, Min.	Streptomycin Solution,* 5,000 Units/Cc. of Isotonic Solution of NaCl		Streptomycin Ointment,† 5,000 Units/Gm. of Ointment Base		Streptomycin Solution, 50,000 Units/Cc. of Isotonic Solution of NaCl	
	Normal Cornea, Units/Cc.	Abraded Cornea, Units/Cc.	Normal Cornea, Units/Cc.	Abraded Cornea, Units/Cc.	Normal Cornea, Units/Cc.	Abraded Cornea, Units/Cc.
15	1	0	0	0	1	20
30	0	8	0	4	0	21
60	1	4	0	30	0	21
120	1	25	1	20	1	14
180	1	3	0	4		
300	0	1	1	1		
360	0	0	0	1		

* Instillation of solutions consisted in administration of a total of 5 drops, 1 every thirty seconds.
† Each instillation of ointment consisted of 0.1 Gm. The ointment base used was Carbowax and propylene glycol.

TABLE 7.—*Concentrations of Streptomycin in Aqueous Humor of Normal Rabbit Eyes Following Local Corneal Iontophoresis* with Solution of Streptomycin Containing 5,000 Units per Cc. of Isotonic Solution of Sodium Chloride*

Time of Puncture of Anterior Chamber After Iontophoresis with Solution of Streptomycin, Min.	Streptomycin, Units/Cc.
30	30
60	70+
90	70+
120	70+

* Iontophoresis consisted in passage of current of 2 mi amperes for three minutes.

COMMENT

It is evident from these data that systemically administered streptomycin penetrated into the aqueous humor and, to a smaller degree, into the vitreous humor of the normal eye. The concentrations in the aqueous and the vitreous humor were increased in the normal eyes by

found in secondary aqueous humor of rabbi and human eyes. With this observation in mind

it would appear that a single injection of 10,000 units per kilogram of body weight systemically administered might produce adequate therapeutic concentrations of streptomycin in the aqueous humor, conjunctiva, sclera and extraocular muscles if these parts were inflamed. However, such a dose would appear to be too small for infections of the optic nerve, chorioretinal tissue, cornea and vitreous, and a dose in the range of 100,000 units per kilogram of body weight would seem more likely to succeed. A satisfactory therapeutic level for ocular infections has not been determined as yet. Such a level will depend largely on the sensitivity to streptomycin in vivo of the individual causative organism. The present study simply indicates the concentrations that can be obtained in the various tissues of the normal rabbit eye and in secondary aqueous humor and may prove helpful in choosing the dose of streptomycin for therapy.

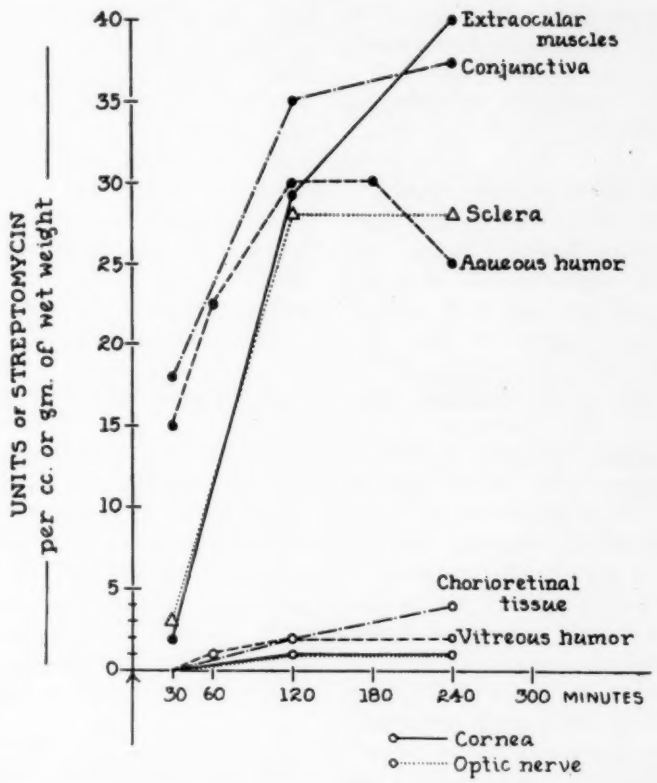
The data here given have shown that locally applied streptomycin in solution and ointment vehicle penetrated poorly into the aqueous humor of rabbit eyes with normal corneas but penetrated well when the epithelial barrier was partially removed, as in corneal abrasions or ulcer. Administration of streptomycin by iontophoresis produced fairly high concentrations in the anterior chamber. Local instillation of drops of a solution containing 5,000 units per cubic centimeter or of an ointment containing 5,000 units per gram will probably prove adequate for therapy of corneal infections due to streptomycin-sensitive organisms.

SUMMARY

A single intravenous or intramuscular injection of 10,000 units of streptomycin per kilogram of body weight produced detectable concentrations of streptomycin in the conjunctiva, sclera, extraocular muscles and aqueous humor of the normal rabbit eye.

The concentrations in these tissues were increased by raising the systemic dose to 100,000 units per kilogram of body weight. With the larger systemic dose, streptomycin also appeared in the cornea, vitreous, chorioretinal tissue and optic nerve of the normal rabbit eye.

Concentrations of streptomycin in secondary aqueous humor were greatly increased over those in primary aqueous humor after systemically administered streptomycin.



Concentrations of streptomycin in the ocular tissues of the rabbit following a single intramuscular injection of 100,000 units per kilogram of body weight.

Local administration in drop form of a solution of streptomycin containing either 5,000 or 50,000 units per cubic centimeter of isotonic solution of sodium chloride or of an ointment containing 5,000 units per gram of base failed to penetrate readily into the aqueous humor of the rabbit eye with a normal cornea. However, both the solution and the ointment penetrated readily into the aqueous humor of the rabbit eye with a partially abraded cornea.

High concentrations of streptomycin were obtained in the aqueous humor of normal rabbit eyes after iontophoresis with a solution of streptomycin containing 5,000 units per cubic centimeter of isotonic solution of sodium chloride for three minutes.

Methods of administration and doses for therapeutic purposes are suggested on the basis of these studies.

Hospital of the University of Pennsylvania.

CONGENITAL CATARACT AND OTHER ANOMALIES FOLLOWING RUBELLA IN MOTHER DURING PREGNANCY

A CALIFORNIA SURVEY

JOHN J. PRENDERGAST, M.D.
SAN DIEGO, CALIF.

A new concept of certain congenital anomalies has developed in the past few years with the discovery of defects in babies born of mothers who had rubella during the first three months of pregnancy. It has been more than a year now since Reese [1] reported 3 cases of congenital cataracts in infants born in the United States of mothers who had rubella in the first month of pregnancy. This report followed the initial ones of Gregg [2] and of Swan and his co-workers,[3] from Australia, who were the first to call attention to these startling conditions. Gradually cases are being recorded by other men throughout the United States, notably Erickson,[4] of Pasadena, Calif., who reported 11 cases in October 1944, and Perera,[5] of New York, who recently reported a case. Winter and Lucic [6] found 9 cases in the pediatric service of a large naval hospital on the west coast.

Several questions immediately confront one in connection with this condition: Is the placental transfer of this virus something of recent occurrence, or has the virus strain been activated in some manner during the past few years to produce these anomalies? Just what is the mechanism of the production of these defects? Why are the eyes, particularly the lens, and the heart affected to a greater degree than are other organs or tissues? Can other virus diseases suffered during these early months of pregnancy result in similar congenital defects in the offspring? What precautions should be taken in a case of rubella occurring in the early months of pregnancy to prevent such sequelae?

That the condition may not be a new one is suggested by Erickson,[6a] who found evidence of it in persons 5 years and 16 years of age, respectively.

Several theories to explain the production of these defects have been suggested, but to date they are all founded on speculation. Much research is still necessary. Gregg [2] expressed the opinion that the majority of cases of rubella concerned in his study occurred during a so-called epidemic in 1940 which affected rather widespread areas in Australia. He further stated that, as reported to him by physicians who cared for the patients, the attacks were rather severe in most cases. This suggested to him that a severe toxic condition was associated with the rubella. Such toxicity certainly has not been associated with the disease in the cases seen in this part of the country. Here, the rubella has occurred in a mild, almost subclinical, form, and in many instances considerable questioning was required to bring out a history of the disease. Therefore, if the virus in the cases of rubella occurring in this country is similar to the virus of the 1940 epidemic in Australia, it would seem that it must be of an attenuated nature. The fact remains, however, that new cases of congenital defects occurring in such circumstances are constantly being reported and that their number is not decreasing.

Of interest to me in discussing cases of this condition with men who have seen many of them is the varying emphasis placed on different types of anomalies or symptom complexes by the different men. The pediatrician is impressed with the malnourished appearance of the infant at birth and with the inevitable feeding problems and lack of normal development. Ophthal-

From the Rees-Stealy Clinic.

Read before the Pediatric Section, California Medical Association, Los Angeles, May 6, 1945.

1. Reese, A. B.: Congenital Cataract and Other Anomalies Following German Measles in Mother, Am. J. Ophth. **27**:483-487 (May) 1944.

2. Gregg, N. M.: Congenital Cataract Following German Measles in Mother, Tr. Ophth. Soc. Australia **3**:35-46, 1942.

3. Swan, C.; Tostevin, A. L.; Moore, B.; Mayo, H., and Black, G. H. B.: Congenital Defects in Infants Following infectious Diseases During Pregnancy, M. J. Australia **2**:201-220 (Sept. 11) 1943.

4. Erickson, C. A.: Rubella Early in Pregnancy Causing Congenital Malformations of Eyes and Heart, J. Pediat. **25**:281-283 (Oct.) 1944.

5. Perera, C. A.: Congenital Cataract Following Rubella in the Mother: Report of a Case, Am. J. Ophth. **28**:186 (Feb.) 1945.

6. Winter, S. J., and Lucic, H.: Personal communication to the author.

6a. Erickson, C. A.: Personal communication to the author.

mologists, of course, were first impressed with the opacities of the lens; now they are beginning to find other ocular defects, such as congenital glaucoma, microphthalmos, pigmentation of the retina, corneal opacities and strabismus. The particular interest of the specialist in the anomalies which fall within his field is to be expected, but the fact remains that the condition is a generalized one affecting the entire organism, especially the eyes and heart.

As to the possibility that other virus diseases during pregnancy may cause similar conditions, one pediatrician, in her reply to my questionnaire reported a case of microphthalmos in an infant whose mother had chickenpox during the early part of pregnancy. She noted that Brennemann,[7] in his "Practice of Pediatrics," classifies chickenpox as a virus disease.

With regard to pathologic changes present in the eye, Swan [8] reported in detail the macroscopic and microscopic observations at autopsy in the cases of 3 infants, and Terry [9] described the changes in the eyes of a baby who had bilateral cataract. Swan found in the left eyes of 2 infants necrosis *en masse* of the nuclear portion of the lens, disintegration of the lens fibers and replacement by vacuoles of various sizes. He noted little formation of new fibers on the posterior part of the lens, where the nucleus was in contact with the posterior capsule. In the right eye of 1 of these infants the anterior epithelial cells of the lens were larger than usual and oval, and he surmised that these cells represented futile attempts at new fiber formation. Terry noted changes throughout the entire eye bilaterally. There were small retinal ganglion cells, a poorly formed meshwork in the angle of the iris and failure of the anterior surface of the iris to undergo atrophy and to produce the usual crypt formation. The ciliary body showed lack of development, and the rods and cones of the retina were poorly developed. The most interesting change, however, was in the lens, where the fetal nucleus almost touched the anterior pole of the lens, indicating that the lens fibers in some manner were prevented from growing forward and inserting themselves in front of the nucleus. This position of the nucleus, as one can see, differs notably from that observed by Swan. In Terry's case the mother had had rubella during the third month of pregnancy.

According to Mann,[10] the preliminary lens fibers begin their development at about the 11 mm. stage, when the embryo is approximately 5 weeks old, and continue until about the 25 mm. stage, when the embryo is 7 weeks old. Then the secondary lens fibers start their development. The ganglion cells first make their appearance at about the 17 mm. stage, when the embryo is approximately 6 weeks old. They have their origin from differentiating cells of the inner neuroblastic layer. The first appearance of the rods and cones takes place at about the 21 mm. embryo stage. The mesodermal stroma of the iris begins to differentiate at the 18 to 20 mm. stage, with the formation of the fetal blood supply and the appearance of the anterior chamber. Thus, it is seen that the outstanding changes noted by Terry [9] are in structures which have their initial process of formation during the second and third months of gestation.

The anomalies in most of the cases of congenital cardiac defects reported were a widely patent ductus arteriosus and a patent foramen ovale. Swan,[8] citing Bedford and Brown, stated that the most important period for the development of congenital defects of the heart is from the fifth to the eighth week of intrauterine life, during which time the septums are forming. Swan pointed out that this was the precise period during which the mothers in his cases suffered from rubella.

According to Brennemann [11] the incidence of uncomplicated congenital lesions of the heart is low, ranging from 0.9 to 6.9 per cent in several large series of autopsies on adults. In autopsies on infants and children, however, the rate is higher, owing, of course, to the fact that the life of children with the more serious cardiac lesions is brief. The incidence of congenital lesions of the heart with associated anomalies elsewhere in the body is high enough (27 per cent in Brennemann's series of cases) to convince one that the same etiologic factor is responsible for the two conditions.

Patent ductus arteriosus is one of the most frequent congenital cardiac anomalies. Normally the ductus arteriosus ceases to function soon after birth, with expansion of the lungs, and is said to be closed completely by the end of the third month. Functional closure of the foramen ovale occurs soon after birth, although anatomic

7. Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1944, vol. 2, chap. 3, p. 1.

8. Swan, C.: A Study of Three Infants Dying from Congenital Defects Following Maternal Rubella in the Early Stages of Pregnancy, J. Path. & Bact. **51**:289-295 (July) 1944.

9. Terry, T. L.: Personal communication to the author.

10. Mann, I.: The Development of the Human Eye, London, Cambridge University Press, 1928.

11. Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1944, vol. 2, chap. 13, p. 35.

closure requires a longer period. Patency of the foramen ovale is the most frequent congenital cardiac lesion, and when it exists alone it is not of great clinical significance.

In the fall of 1944, a survey was made among some of the ophthalmologists, pediatricians and obstetricians in California to obtain an idea of the incidence of congenital anomalies among children in this state whose mothers had had rubella during the first three months of pregnancy. Replies were received from 37 ophthalmologists, 24 pediatricians and 32 obstetricians, and their data are tabulated in the accompanying tables. Undoubtedly, some duplication is present, as in cases in which the same patient may have been seen by two physicians, for example, the ophthalmologist to whom the patient was referred and the attending pediatrician; and for this reason the numbers of cases reported by the ophthalmologists, pediatricians and obstetricians respectively are given separately in table 1. Furthermore, since not all the men who might see children with such defects were reached, the figures cannot be considered complete. In this survey, a total of 80 cases of congenital cataract and 10 cases of other ocular defects (table 1 A), 32 cases of cardiac defects (table 1 B) and 10 cases of other congenital anomalies (table 1 C) were reported. It is in the group of ocular defects that the greatest amount of duplication probably exists. Table 2 shows that 10 cases of rubella in women during the first three months of pregnancy were reported by the obstetricians and that congenital defects were present in 6 of the children of these mothers.

TABLE 1.—*Congenital Defects in Children Whose Mothers Had Rubella During First Three Months of Pregnancy*

	No. of Cases
A. Ocular Defects	
Cataract reported by ophthalmologist	40
Cataract reported by pediatrician	35
Cataract reported by obstetrician	5
Congenital glaucoma (reported by ophthalmologist)	2
Strabismus (reported by ophthalmologist)	1
Microphthalmos (reported by pediatrician)	4
Pigmented retina (reported by pediatrician)	2
Corneal opacity (reported by pediatrician)	1
B. Cardiac Defects	
Lesion reported by pediatrician	27
Lesion reported by obstetrician	5
C. Miscellaneous Anomalies	
Mental retardation (reported by pediatrician)	3
Mental retardation (reported by obstetrician)	1
Severe anemia (reported by pediatrician)	1
Purpura (reported by pediatrician)	1
Microcephalos (reported by pediatrician)	1
Hypospadias (reported by pediatrician)	1
Cleft palate (reported by pediatrician)	1
Inguinal hernia (reported by pediatrician)	1

TABLE 2.—*Cases of Rubella in Mothers During First Three Months of Pregnancy**

Total no. of cases	10
No. of offspring with congenital defects	6
	No. of Cases
Congenital cataract	5
Congenital cardiac defect	5
Congenital mental deficiency	1

* Reported by obstetrician.

Because the greater number of cases to date has been reported from the western part of the United States, one wonders whether such congenital defects are more prevalent in this part of the country or whether, like the epidemic of shipyard conjunctivitis of several years ago, which started in Hawaii, spread to the Pacific coast and thence to the rest of the United States, this condition has spread to the Pacific coast from Australia, where it was first reported, and is now making its way across the country. Further surveys will be of interest from this point of view also.

SUMMARY

A brief review of the reported cases of congenital defects in children born of mothers who had rubella during the first three months of pregnancy is given. The pathologic observations in the cases of congenital cataract and the possible significance of the time of development of these anomalies in the embryo are discussed. The results of a survey made among some of the ophthalmologists, pediatricians and obstetricians in California to obtain an idea of the incidence of cases of these defects in the state are reported.

2001 Fourth Avenue.

OCULAR IMAGERY

ALFRED COWAN, M.D.
PHILADELPHIA

In von Helmholtz's "Treatise on Physiological Optics," [1] Gullstrand, prefacing the description of his investigations of the actual imagery of the eye, made the following statement:

> . . . The theory of collinear imagery applied to objects of finite extent and stops with finite apertures, which is the basis of the expositions still to be found in modern text-books, constitutes . . . an essentially arbitrary extension of the region of validity of these laws, inasmuch as a system of fictions had to be introduced in place of the ideal undiscovered law.

A misunderstanding of what Gullstrand meant seems to have caused considerable concern among some ophthalmologists. For instance, Lancaster,[2] concerning Gullstrand's statement, said:

> . . . Then a prophet appeared and proclaimed the errors that permeated the current belief and practice. . . . I believe the time is ripe for teaching ophthalmologists the truth about the formation of images . . . the present methods of teaching that subject have been a failure.

But Gullstrand did not give a better way of teaching physiologic optics, and neither has any one else. Gullstrand did not mean that what he called the "system of fictions" should be discontinued for teaching. He said, and rightly, that one should avoid overstepping the border between what is true and what is nearly true, by representing the realities as aberrations or deviations from the ideal relations of collinear correspondence. All competent teachers of physiologic optics do that.

The fundamental laws of reflection and refraction are correct, and for an infinitely narrow, paraxial bundle of rays the theory of collinear imagery is valid. Sturm's theorem, even if fundamentally false, especially in its application to the eye, is far too valuable a means of illustrating the passage of light through an astigmatic system to be discarded. No less an authority than Southall[3] said:

> . . . In spite of its limitations and admittedly imperf representation, Sturm's conoid remains a very use preliminary mode of conception of the character of narrow bundle of rays

Gullstrand also branded the nodal points, principal planes and the principal focal planes so much useless ballast, but not for teaching.

There is no reason that fictions should not employed if they serve to enable the stude better to understand a subject. Gullstrand hi self never hesitated to use them. His schema eye is nothing but a mathematical conception, constants of which are calculated for an infinite narrow, paraxial bundle of rays. Surely, no o believes that the distances of the cardinal poi along the axis, measured to the thousandth a the ten thousandth of a millimeter, are meant be actualities. The structure of his lens is pure theoretic. Even the aberration of 1 D. which gave his eye is only an approximation. He use when it sufficed to illustrate a point, Donder reduced eye, the simplest of all eyes, and a pu fiction. An infinitely thin lens is a fiction, Gullstrand used it in his simplified schematic ey A mathematical point of light is a fiction.

What Gullstrand really meant is that Gauss theory of collinear image points and the foc lines in the conoid of Sturm hold only in the ca of an infinitely narrow bundle and are not use when applied to the actual imagery of objects finite extent and stops with finite apertures, esp cially an eye: They could not be used in his sp cial investigation of the determination of th actual pattern of the caustic of the dioptric sy tem of the eye. In order to do this more scienti cally, he made a study of the construction of bundle of rays in general and also of the law of optical imagery in heterogeneous medium Instead of the notion of focal lines, he used h method of infinitesimal, or differential, geometr Direct examinations were carried out with wh he called subjective and objective stigmatoscop His investigations were the most thorough scientific studies of the convergence of the ra in the eye, the monochromatic aberrations a the actual form of the caustic that have ever be made.

But long before Gullstrand was born Thom Young (1801) showed conclusively that t

1. von Helmholtz, H.: Treatise on Physiological Optics, translated and edited by J. P. C. Southall, Ithaca, N. Y., Optical Society of America, 1924, pt. 1, appendix, p. 262.

2. Lancaster, W. B.: The Story of Asthenopia, Arch. Ophth. **30**:167 (Aug.) 1943.

3. Southall, J. P. C.: Mirrors, Prisms and Lenses, New York, The Macmillan Company, 1918, p. 535.

eye was neither achromatic nor aplanatic. Many other investigators, particularly Volkmann (1836), Donders (1864), Herman Knapp (1864) and Tscherning (1898), had already investigated the monochromatic aberrations of the eye, often with the use of a point of light. Gullstrand's objective stigmatoscopy is nothing more than a refinement of Edward Jackson's [4] technic of skiascopy with a luminous point.

In the eye and in the most carefully corrected optical lens systems the best image of a point object is a circle of confusion, never a point. It is a small but measurable area, a diffusion image, in which there is a tremendous confusion produced by all the phenomena natural to light; but in any optical system, as well as in the eye, the distinctness of the image is inversely proportional to the resolving power, and as long as the diameter of the diffusion image is no greater than the resolving power the image will be distinct.

The eye possesses all the aberrations of a spheric lens with the added faults of the asymmetry and decentrations of the refracting surfaces and the heterogeneous nature of the media of a living organ. Modern lens designers can produce an almost perfectly corrected lens for a specific purpose. Yet, although the aberrations of a symmetric artificial optical system are relatively simple as compared with those of the eye, an artificial image-forming instrument that would correspond with and serve all the needs of a human eye is impossible to attain.

The caustic produced by the convergence of rays in the eye is an extremely intricate, three dimensional form, which Gullstrand [5] concluded has three cusps in its meridional section. He stated that because of the complicated form of the caustic it is a mathematical impossibility for any cross section to cut the surface in a smooth curve, in the form of a circle concentric with the pupil. On the contrary, this section must be serrated everywhere or must consist of separated isolated points. He showed the aberration in the eye to be so great and the diffusion images so large that the most useful image could not possibly correspond to the narrowest cross section of the bundle, because shades of brightness are of more importance than absolute brightness. This is in agreement with Tscherning,[6] who also stated the belief that the best visual acuity is obtained where the section of the caustic is smallest, not where the cone has the least diameter (the point of the arrow). But Ames and Proctor [7] stated definitely that the eyes they investigated focused where the cone has the least diameter. They found also that the aberration was considerably less than that given by Gullstrand. The aberrations of the eye vary with the individual, with the size of the pupil, with the intensity of illumination and with accommodation.

The results of all such investigations are interesting academically; but, whatever the shape of the diffusion image, regardless of the complicated nature of the aberrations and the intricate pattern of the caustic produced or of whether the cusp or any other part of the caustic is utilized, this image will answer the purpose of a point image as long as its diameter is no greater than the resolving power of the optical system.

The eye will choose, either by accommodation or by the selection of a lens, that part of the caustic which gives the most distinct visual acuity, and, since sharp vision is obtained only in the vicinity of the fovea, that part of the convergent pencil which best answers the purpose will be selected. Central visual acuity is dependent on the distinctness of that very small portion of the image which lies in the area of the fovea. The surrounding halo is already in the periphery and is disregarded by the eye. Also, the peculiar structure of the retina practically neutralizes marginal astigmatism, curvature of field, distortion and other faults. The modern camera lens, so marvelously designed that a clear image is produced out to the edge of the plate, does not apply to the eye. Not only would such an image be useless; it would be confusing.

The faults of the dioptric system of the eye do not interfere with distinct visual acuity. In the words of Gullstrand,[7a]

> . . . the monochromatic aberrations are a witness for the perfection of the eye, if what is meant by the perfection of an optical instrument is good convergence of rays to the degree that is needed to obtain the greatest useful sharpness of image: anything in excess of this being sacrificed in order to gain some other end.

The aberrations of any optical system increase with the diameter of the aperture. With a small pupil there are less aberration and greater focal depth, but less brightness; and if very small, even with adequate illumination, the beneficial effect of the narrow aperture is overcome by the diffraction at the edges. The pupil must be large enough to afford sufficient brightness and at the same time to allow the formation of a sharp image by the effect on the resolving power of the eye.

4. Jackson, E.: Skiascopy, Philadelphia, Edwards & Docker Co., 1895.

5. Gullstrand, in von Helmholtz,[1] p. 462.

6. Tscherning, M.: Physiologic Optics, translated by C. Weiland, Philadelphia, Keystone Publishing Co., 1924, pp. 129-130.

7. Ames, A., and Proctor, C. A.: Aberrations of the Eye, Am. J. Physiol. Optics **4**:3, 1923.

7a. von Helmholz,[1] p. 443.

Theoretically, the pupil must be neither too wide nor too narrow. The resolving power is fairly constant as long as the diameter is between 3 and 5 mm. (Southall.[8] Because of the peculiar nature of the eye as an optical instrument, a large pupil has little or no effect on the distinctness of the useful retinal image as long as the system is properly in focus, whether normally, by the accommodation, or by the aid of a lens. A small pupil serves its best purpose when the image is not sharply focused.

In ocular refraction the importance of the action of the pupil must not be overlooked. Only by the use of a cycloplegic can both the accommodation and the activity of the pupil be kept under control, and, theoretically, no method of refraction, objective or subjective, is absolutely reliable with an active pupil.

Since only a relatively small bundle of rays, close to the visual axis, goes to form the useful retinal image, it is often stated, and rightly, that with a large pupil the aberration a short distance from the axis sometimes seriously interferes with the results of retinoscopy. In most cases this fault can be eliminated by having the patient fixate the center of the mirror so that the examiner, disregarding the peripheral reflexes, can measure the error along the visual axis. This cannot be done precisely with noncycloplegic methods of retinoscopy.

In any subjective examination a wide, inactive pupil is a distinct advantage. The eye, then, without the power of accommodation and without a sufficiently small stop aperture to affect either the depth of focus or the aberration, is enabled to obtain its best visual acuity only by the aid of the proper correcting glass.

8. Southall, J. P. C.: Introduction to Physiological Optics, London, Oxford University Press, 1937, p. 79.

It is logical to infer from a consideration of the phenomena under discussion that objective methods for the determination of the refraction of the eye are only an approximation, in many instances a very close one, but nevertheless an approximation. In no case should the objective results be depended on when a subjective examination is possible. The most accurate measurement of the refraction is determined by that lens which produces the sharpest retinal image in the static eye. No matter what method is used, the correctness of the refraction must be measured by the lens that procures for the static eye the best visual acuity at a distance.

The ophthalmologist in the practice of ocular refraction should have a proper conception of the convergence of the rays in the eye, of the physiologic characteristics and nature of the eye in the selection of the most useful surface of the caustic, and of the role of the pupil, all in order that the eye may procure the best visual acuity possible. With such knowledge he can appreciate the marvelous adaptability of the human eye, which in spite of its many imperfections is still superior to the most carefully designed artificial instrument. Also, he will be in a position to judge for himself of the value of each procedure for the determination of the refraction. There are many useful methods, every one of which will be found to have some disadvantage in certain cases. There is no one method that should be used to the exclusion of all others, whether for the determination of the spheric or of the astigmatic error.

The closest approximation to the exact correction of ametropia should be the aim of the ophthalmologist; but his knowledge of physiologic optics will enable him not only to secure the best result but to know when further exactness is superfluous. Perfection is neither possible nor necessary in an instrument so adaptable as the eye.

1930 Chestnut Street.

Clinical Notes

RETINAL VENOUS THROMBOSIS FOLLOWING REACTION TO VACCINE

Report of a Case

CAPTAIN PARKER M. HOFFMAN
MEDICAL CORPS, ARMY OF THE UNITED STATES

Venous thrombosis of the retina is a condition rarely seen in young soldiers after vaccination. This case is the first to occur in my experience and presents interesting clinical features. The earliest examination of the fundi was made one week after onset of symptoms.

REPORT OF A CASE

A 21 year old white soldier was given subcutaneous injections of 1 cc. of typhus vaccine and 0.5 cc. of triple typhoid vaccine (stimulating doses) on March 3, 1945. Intradermal vaccination for smallpox was also done on the same date. One year previously he had received simultaneous inoculations for cholera and typhus and, later, simultaneous inoculations for yellow fever and typhoid, without systemic reactions. He had never before been given typhus and typhoid vaccines on the same day. He had received his last previous injection of a stimulating dose of cholera vaccine on Jan. 5, 1945. His first reaction to vaccine occurred after the injections on March 3 and was characterized by onset of severe aching of the muscles and joints and general prostration three or four hours after the injections. Although the temperature was not read, it is likely that a low grade fever accompanied the reaction, which had entirely subsided by the following morning. At this time he felt fine. He had an immune reaction to smallpox vaccine.

On the afternoon of the second day he first noticed blurring of vision in the inferior field, which disappeared on occlusion of his left eye. He reported to his medical officer one week later, when the blurring failed to improve. He had experienced no other ocular symptoms and felt well in general. He was admitted to the hospital for study on March 10.

Vision had always been good in both eyes, and he gave no history of previous ocular ailments or injuries. Except for a fracture of the left femur in childhood, which healed normally, he had always had excellent health. His family history was noncontributory.

On physical examination he appeared well developed and well nourished. Medical examination revealed no abnormalities of the chest, the blood pressure or the cardiovascular, genitourinary or other systems. No possible foci of infection in the teeth, throat, sinuses or prostate gland could be found. Laboratory studies, including a Kahn test of the blood, a complete blood count, determination of the bleeding and clotting times and the sedimentation rate and urinalysis, all gave results within normal limits. A roentgenogram of the chest and the electrocardiogram were normal. The temperature and pulse remained normal.

Initial ophthalmic examination revealed vision of 20/20 in each eye. There was no evidence of trauma or disease of the external ocular structures. The pupillary reactions were normal. The media and fundus of the right eye were normal. There was mild turbidity of the vitreous in the left eye. The disk was clearly outlined, and the retinal arteries appeared of normal caliber and luster. The main superior temporal vein of the retina of the eye, together with most of its tributaries, was partially obscured, beginning 1 disk diameter above its entrance into the papilla. Portions of the veins which could be seen through the dense hemorrhages and exudates were tortuous and cordlike. The main inferior temporal and superior nasal veins presented several areas of periphlebitis at bifurcations and arteriovenous crossings. A white sheathing of the terminal tributaries of these veins by exudates was observed. The macula was not involved, although there were a few small hemorrhages just temporal to it and some very tortuous macular veins just above it. The accompanying diagram of the temporal portion of the fundus (fig. 1) indicates these changes, as seen on initial examination. The intraocular tensions were normal and equal in the two eyes and remained constantly so, as determined by frequent tonometric readings.

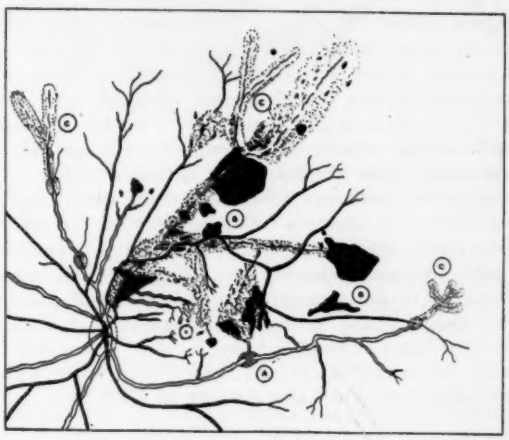


Fig. 1.—Early appearance of the temporal portion of the left fundus. *A* indicates the area of periphlebitis and the point of subsequent thrombosis; *B*, retinal hemorrhages, and *C*, perivenous exudates.

From the initial examination and from the patient's history it was assumed that the main superior nasal and temporal veins and the main inferior temporal vein of the left eye had been attacked by an acute endophlebitis, the superior temporal vein having become thrombosed soon after onset of the symptoms. One week after initial examination the main inferior temporal vein became thrombosed at a point of previous constriction. Three days later signs of optic neuritis, namely, papillary edema, changes in the fields and reduced vision, of 20/100, appeared in the left eye. A week later a broad hemorrhage appeared above the macula, with small hemorrhages and pigmentary changes in the macula itself. This hemorrhage was evidently due to an extension of the thrombotic process of the main superior temporal vein to occlude completely its small central tributaries. Vision in the affected eye continued to diminish until it was limited to perception of form at 1 foot (30 cm.).

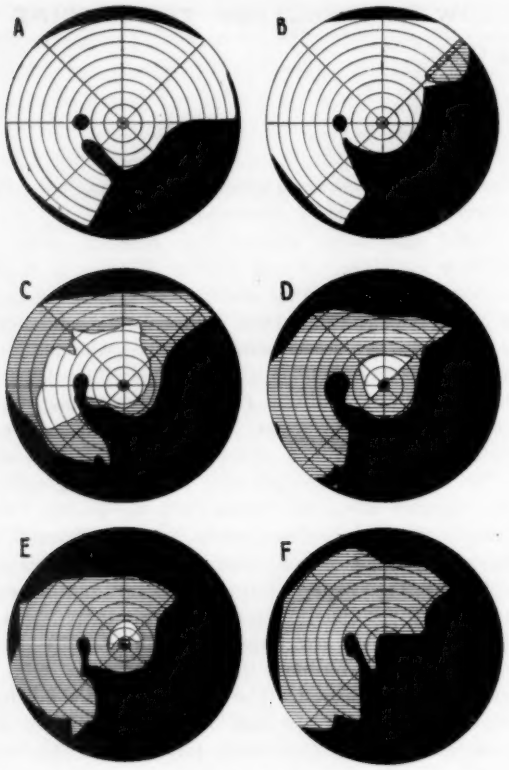


Fig. 2.—Visual fields of the left eye taken with the tangent screen. *A* (March 10), initial scotoma in the inferior nasal field, vision 20/20; *B* (March 17), enlargement of the scotoma with a relative component due to thrombosis of the inferior temporal vein, vision 20/30; *C* (March 21), enlargement of the blindspot, small central scotoma and peripheral contraction due to secondary optic neuritis, vision 20/100; *D* (March 23), progressive narrowing of the visual fields, vision 20/100; *E* (March 25), changes following cervical sympathetic nerve block, vision 20/200, and *F* (April 7), extension of the scotoma following thrombosis of the central tributaries of the superior temporal vein, with macular hemorrhage, vision limited to perception of form at 2 feet (60 cm.). Fields *A* to *E* were taken with a 3 mm. white test object and field *F* was taken with 6 mm. white test object at a distance of 1,000 mm.

The patient was treated with potassium iodide, and the older hemorrhages began to absorb. Three cervical sympathetic nerve blocks were employed for treatment of the optic neuritis. Procaine hydrochloride (1 per cent) with epinephrine hydrochloride (1 : 50,000) was used, with good peripheral vasodilatation. During the period of observation the disk became more sharply outlined and the blindspot assumed its normal size. Tangent screen charts (fig. 2) indicate the progressive changes in the field which paralleled the rapid advance of the pathologic process. After a period of two weeks in which there was relatively little change, the patient was transferred to the Zone of the Interior for further follow-up study and treatment.

SUMMARY

The uncommon occurrence of retinal periphlebitis and progressive thrombosis in a young adult following stimulating doses of vaccines with associated anaphylactoid reaction is recorded with a case history.

The early stage of involvement of the inferior temporal veins was apparent, and progressive thrombotic changes in the fundus and visual fields were followed. It is of interest that the superior nasal veins, although showing similar early periphlebitic constrictions and exudate, did not become thrombosed, and the exudate disappeared completely. Optic neuritis occurred in the affected eye during the third week of the disease, followed one week later by macular involvement. Intraocular tension was not notably affected during my six weeks' observation of the patient.

Clinical Notes

CORNEAL PUNCH FOR SQUARE AND RECTANGULAR TRANSPLANTATIONS OF CORNEA

CONRAD BERENS, M.D., NEW YORK

When one is performing transplantations of the cornea using a rectangular implant, a protruding lip of cornea may remain posteriorly. This condition is especially likely to be encountered when the recipient cornea is thickened or edematous. The removal of this lip with instruments ordinarily available has been found most difficult. Therefore a square corneal punch has been devised.[1] It has been in use since 1941 and has been found practical in performing square and rectangular transplantations of the cornea.

The lower blade of the punch, which is introduced into the anterior chamber, is rounded

Fig. 1.—Square keratoplasty punch.

and dull, so that danger of injury to the lens is minimized. The double action of the cutting blade reduces the force required to snip the cornea. The punch cut is made from above downward, and the lower blade of the forceps remains stationary. After the area to be grafted has been excised, any lip of cornea which remains is removed, as shown in figure 2.

The punch may be used for excising the sclera in iridocorneosclerectomy,[2] but the use of the rounded cutting blade previously described[2] is

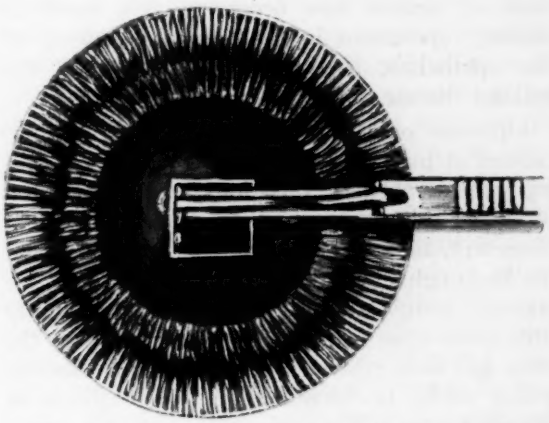


Fig. 2.—After the area to be grafted has been excised, any remaining lip of corneal tissue is clipped with the square corneal punch. A second bite of cornea is being excised with the punch.

preferred for sclerectomy and for the excision of irregularities in the recipient cornea when preparing for circular grafts.

35 East Seventieth Street (21).

This study was aided by a grant from the Ophthalmological Foundation, Inc. Construction of the instrument was also aided by a grant from the John and Mary R. Markle Foundation.

1. The instrument was made by V. Mueller & Co., Chicago.

2. Berens, C.: Iridocorneosclerectomy for Glaucoma, Am. J. Ophth. **19**:470-481, 1936.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

OCULAR COMPLICATIONS OF MALARIA

W. MORTON GRANT, M.D.
BOSTON

The incidence of ophthalmic disease is significantly increased in patients with malaria, and the ocular disturbance can at times be the most serious complication of the general illness. This is an opinion borne out by more than 200 reports on the ocular complications of malaria published in the past seventy years. Certain types of ocular lesions appear to be characteristically associated with the various phases of systemic malarial infection. In view of the number of new cases of malaria now occurring as a result of military operations in the tropics, a survey of the ophthalmic aspects of the acute and the masked disease appears pertinent.

Opinions on the frequency of ocular complications in malaria have been divergent, depending considerably on variations in the definition of the term "complication" used by the different observers, as well as on the type of disease and the thoroughness of examination. In some instances "complication" has been used to signify little more than coincidence, while in others the term has been restricted to those ocular lesions which could be identified as local effects of the plasmodia. The patients described in some reports were seriously ill or were moribund. A number of factors must, therefore, be taken into consideration in examining the literature for information on those aspects which seem to be of most practical importance now, i. e., changes in eyes which may occur as the result of the development of acute or masked malaria in otherwise healthy persons. On inspection of the figures available for the incidence of ocular complications from this standpoint, it appears that the values of 10 per cent (Poncet,[1] 1878) and 20 per cent (Sulzer,[2] 1890), which applied to a selection of chronically and seriously ill patients, might be excessive, whereas the opinion of Elliot,[3] that ocular manifestations were rare in India, was influenced by a reluctance to consider as a complication of malaria any ocular disease unless it could be demonstrated to be caused directly by the plasmodium (by biopsy or necropsy), or at least to be cyclic in nature and alleviated by quinine. Experiences in Africa and Greece in World War I applied largely to new acute infections in Europeans acquired in this course of military migrations and should be more closely analogous to present conditions, except, of course, for current improvements in the treatment of the systemic disease. In caring for troops in Salonika, Bywater[4] (1922) was impressed with the fact that there were comparatively many ocular complications in the cases of malaria but scarcely any in an equal number of cases of dysentery seen at the same time. Dedimos[5] (1932), reporting in detail his observations on French soldiers infected with malaria in Macedonia, stated that the incidence of ocular complications was between 10 and 20 per cent, while Carlotti[6] (1918), for the same period in Greece, indicated nearly 10 per cent. More recently an incidence of 15 to 20 per cent has been reported from Brazil (Fialho,[7] 1927). On the other hand, Toulant[8] (1938), from his experiences in a civilian hospital in Algiers with several hundred patients suffering from chronic or cachectic malaria, concluded that ocular complications were relatively infrequently attributable to malaria and that most of the ocular disease was due to syphilis, alcoholism, quinine poisoning and trachoma. In general, it would be expected that the relationship between ocular

From the Howe Laboratory of Ophthalmology, Harvard Medical School.

1. Poncet, F.: De la chorio-rétinite palustre, Ann. d'ocul. **79**:201, 1878.

2. Sulzer, D. E.: Trouble de la vision dans l'impaludisme, Arch. d'opht. **10**:193, 1890.

3. Elliot, R. H.: Tropical Ophthalmology, New York, Oxford University Press, 1920.

4. Bywater, H. H.: Notes on Malarial Condition of the Eye, Tr. Ophth. Soc. U. Kingdom **42**:359, 192

5. Dedimos, P.: Les manifestations oculaires du paludisme, Arch. d'opht. **49**:166, 249 and 330, 1932.

6. Carlotti: Troubles de l'appareil visuel attribuable au paludisme en Macédoine, Ann. d'ocul. **155**:478, 191

7. Fialho, A.: Manifestaçoes oculares do paludismo, Arch. brasil. de med. **27**:162, 1927.

8. Toulant, P.: Complications oculaires du paludisme, Acta ophth. orient. **1**:18, 1938.

ease and malaria might be most clearly distinguished in young men medically preselected military service, among whom the incidence complicating systemic disease is normally low. counts of experience with ocular complications World War II by Talbot [9] (1943) and Robertson [10] (1944) give the impression that ocular anifestations are relatively frequent, although, fortunately, actual figures are not cited. In nsideration of the opinions and evidence preted in these various reports, it seems reasonle to conclude that malaria is worthy of note an inciter of ocular disturbances.

The several types of ocular complications hich have been associated with malaria are in eneral described with considerable uniformity numerous observers. The most frequent ular complication has been considered, almost nanimously, to be dendritic, or herpetic, keratis.[11] This corneal disease has constituted a nsiderable proportion of the ocular disease sociated with malaria reported by various authors from the time of its recognition in conunction with malaria by Kipp,[12] in 1880, to the ecent observations on troops in the southwest Pacific by Chamberlain and Bronson.[13] Series cases of herpetic keratitis associated with malaria have been reported by Kipp [14] (1889, 20 cases), Chavernac [15] (1918, 146 cases), Bywater [4] (1922, 60 cases), Kiep [16] (1922, 63 cases) and Carlotti [6] (1918, 46 cases). Much less often nterstitial keratitis has been noted. Neither form of the corneal disease has been shown to be ue to a local infection with plasmodia. More ecently, herpetic keratitis was observed by Chamberlain and Bronson [13] (1945) to occur six times as frequently in a division in which 0 per cent of the soldiers had malaria as in a comparable group which was free from malaria. Although this complication was found in only 1 of every 700 patients with malaria, it ranked above any other single ocular condition as a reason for limiting duty, because of persistent irritation and interference with vision. The type of malaria most commonly causing this corneal disturbance is the benign tertian form. The dendritic keratitis appears characteristically twenty-four to forty-eight hours after a first attack of malarial fever, although it also often occurs with subsequent attacks of fever or between attacks.[8] The keratitis usually occurs in one eye only, and its onset is marked by discomfort, ranging from the sensation of a foreign body to burning with photophobia and lacrimation. The cornea is hypesthetic, and the lesion stains with fluorescein in the typical dendritic pattern recognized as a characteristic manifestation of the herpes simplex virus in the corneal epithelium. The virus has been identified in the condition associated with malaria. The usual course of the keratitis in the absence of local treatment is gradual improvement over a period of approximately six weeks, with residual corneal opacification and often with recurrences of the process. Treatment of the lesion with iodine ordinarily shortens the course, and recent evidence indicates that application of sulfadiazine powder may be beneficial.[17] It appears likely that the hyperthermia of the acute febrile attacks may incite the corneal disease in malaria, since herpetic keratitis also occurs with other illnesses characterized by fever, such as infections of the respiratory tract, pneumonia and influenza. Another possible inciting factor, which will be discussed in more detail subsequently, is malarial trigeminal neuralgia.

Besides the herpetic keratitis already described, a type of corneal lesion referred to by most authors is described as a monocular interstitial process with clouding of the stroma but without vascularization.[18] However, this second type of corneal lesion appears to be relatively rare even with chronic and cachectic malaria. Severe forms of the condition have been described as keratitis profunda [19] and disciform keratitis.[20] The epithelium is said to be essentially normal except for small, subepithelial opacities or in-

9. Talbot, D. R.: New Aspects of Malaria, J. A. M. A. **123**:192 (Sept. 25) 1943.

10. Robertson, J. N.: Ophthalmologic Lesions Encountered in Tropics, with Special Reference to Ocular Manifestations of Malaria, North Carolina M. J. **5**: 483, 1944.

11. (*a*) Bispham, W. N.: Malaria, Baltimore, Williams & Wilkins Company, 1944. (*b*) Fialho.[7] (*c*) Toulant.[8]

12. Kipp, C. J.: On Keratitis from Malaria Fever, Tr. Am. Ophth. Soc. **3**:91, 1880.

13. Chamberlain, W. P., and Bronson, L. H.: Herpes Simplex Keratitis in Malaria, Arch. Ophth. **33**:177 (March) 1945.

14. Kipp, C. J.: Further Observations on Malarial Keratitis, Tr. Am. Ophth. Soc. **5**:331, 1889.

15. Chavernac, P. L.: Les complications oculaire du paludisme a l'armée d'Orient, Marseille méd. **55**:209, 326 and 376, 1918.

16. Kiep, W. H.: Ocular Complications Occurring in Malaria, Tr. Ophth. Soc. U. Kingdom **42**:394 ,1922.

17. Gundersen, T.: Herpes Corneae, Arch. Ophth. **15**:225 (Feb.) 1936. Chamberlain and Bronson.[13]

18. (*a*) Blatt, N.: Augenveränderungen bei Malaria, Klin. Monatsbl. f. Augenh. **80**:468, 1928. (*b*) Dedimos.[5] (*c*) Kiep.[16] (*d*) Bywater.[4]

19. von Arlt, F. R., cited by Fuchs, E.: Text-Book of Ophthalmology, translated by A. Duane, Philadelphia, J. B. Lippincott Company, 1911.

20. Maxwell, E. M.: Observations on Eye Conditions Met with in Malta, 1916-1917, Brit. J. Ophth. **2**:406, 1918.

filtrates in some instances.[6] The process is accompanied with intense vascular injection about the cornea. Pathogenic organisms have not been found in the conjunctival sac. There are photophobia, fronto-orbital pain and reduction of vision. Progress is slow; the inflammation usually lasts two to three months and may leave permanent corneal opacity. The nature of the pathologic processes concerned in the production of this type of keratitis is undetermined. However, in view of the frequency of herpetic keratitis, it seems possible that some of the interstitial lesions may be metaherpetic sequelae.[17]

A major proportion of the ocular complications which have been described in association with malaria are due to vascular and neurologic lesions. These disturbances are apparently dependent on the pathologic changes in small vessels which are considered to be an important feature of malarial infection, especially in the more severe forms of the disease, e. g., the malignant tertian type (Kirk,[21] 1918; Bywater,[4] 1922). The microscopic characteristics of minute foci of necrosis and hemorrhage, resulting from degenerative changes in capillary endothelial cells and obstruction of the lumen of the vessel by pigmented leukocytes and erythrocytes, have been described in the eye by Poncet [1] (1878) and in the brain by Dürck [22] (1925). The vascular lesions of the brain associated with malaria which are considered to be closely analogous to those of the eye have been reviewed in detail by Anderson [23] (1927). Endothelial changes are described, including phagocytic action, degeneration and hypertrophy, with capillary obstruction by parasitized erythrocytes and leukocytes, free pigment and endothelial cells. The tendency to capillary thrombosis in malaria is partly explained by an increased agglutinative tendency of parasitized erythrocytes.[24] Pigment arising from parasites and degenerated erythrocytes may be found deposited in the neighborhood of small vessels, especially in cases of chronic or cachectic malaria, but appears to be of little significance when not causing obstruction. The suggestion made by some authors of a "toxic" factor in the production of injury to blood vessels is based on the occasional observation of degenerative changes in vessel walls without thrombosis.[25]

Hemorrhages in the ocular fundus, presumably resulting from malarial alterations in vessel walls, have been noted by many observers. Two types of retinal hemorrhage are usually described, a small peripheral and the large central.[26] The latter type, which may destroy central vision, is practically limited to chronically recurring cachectic malaria with severe anemia and appears to occur rarely at present. The small type of hemorrhage, which characteristically is multiple and located in the periphery of the retina, is believed to be more common in occurrence even in the less severe malarial infections. Owing to the location of the lesions, in the neighborhood of the ora serrata, visual disturbances are not observed, and the presence of hemorrhages themselves may not be detected unless careful ophthalmoscopic examination is made. Some idea of the incidence of retinal hemorrhages in unselected cases of malaria may be obtained from the observation by Kiep (1922) of 10 instances of this lesion during a period in which he encountered 63 cases of malarial herpetic keratitis (among soldiers in World War I). The retinal vascular lesions have been noted most often in association with malignant tertian (tropical) malaria, and an increase in the number of hemorrhages during an acute exacerbation of fever has been frequently described.[18a] It is concluded by most observers that the small type of retinal hemorrhage is readily reabsorbed under antimalarial treatment and rarely leads to retinitis proliferans or retinal separation.[28] When the malaria is of fatal severity, retinal hemorrhages are reported to be a constant histologic feature and are presumed to be caused by multiple embolic or thrombotic occlusions of small vessels, analogous to the process believed to underlie the formation of the cerebral petechial hemorrhages observed with this disease.[29] Emptying of retinal vessels peripheral to emboli was described by Poncet (1878) from a study of flat preparations of retinas of malarial patients, and it is possible

21. Kirk, J.: Malaria and Diseases of the Eye, Brit. M. J. **2**:110, 1918.

22. Dürck, H.: Ueber die mit herdförmigen Gliaproduktionen einhergehenden Erkrankungen des Nervensystems, Arch. f. Schiffs- u. Tropen-Hyg. **29**:43, 1925.

23. Anderson, W. K.: Malarial Psychoses and Neuroses: Their Medical, Sociological, and Legal Aspects, New York, Oxford University Press, 1927.

24. Bignami, A., and Nazari, A.: Sulle encefaliti emorragiche e sulla patogenesi delle emorragie miliariche del cervello, Riv. sper. di freniat. **62**:109, 1916.

25. Anderson.[23] Blatt.[18a]

26. (*a*) Villard, H.: Les complications oculaire du paludisme, Arch. d'opht. **47**:200, 1930. (*b*) Poncet.[1] (*c*) Toulant.[8] (*d*) Blatt.[18a]

27. Elliot.[3] Bywater.[4]

28. (*a*) de Andrade, C.: Augenabteilungen bei den Tropenkrankheiten, Arq. clin. oftal. **4**:17, 1937. (*b*) Motegi, A.; Kan, T.; Kó, S., and Syú, S.: Ophthalmologische Beobachtungen an 100 Fällen von Malaria-Kranken, Klin. Monatsbl. f. Augenh. **92**:797, 193[illegible] (*c*) Blatt.[18a]

29. Anderson.[23] Poncet.[1]

that an apparent spasm of retinal vessels accompanying hemorrhages and amaurosis, which has been described in a few instances, may be a manifestation of such embolic obstruction, although the association of changes in retinal vessels with peripheral ischemia noted by Raynaud in a case of malaria suggested a truly spastic condition.[30] Plasmodia have been identified in the vascular lesions of the retina by Laveran[31] (1880) and Fisher[32] (1921) and in vessels of the optic nerve and retina by Dudgeon[33] (1921). The same kind of malarial lesions which may be found in blood vessels of the retina and brain are also found in the vessels of the choroid and optic nerve.[34] In the fatal cases studied by Poncet[1] (1878) choroidal vessels were usually distended with erythrocytes and pigment-containing leukocytes. Accumulations of extravasated phagocytic cells were present in some places. Edema was conspicuous, especially in the region of the papilla. In cases in which the systemic disease is of much less severity than it was in Poncet's cases, evidences of similar choroiditis or chorioretinitis may be found clinically in the fundus in the form of edema, particularly the peripapillary type, followed in some instances by the appearance of yellowish white patches with smaller accumulations of pigment (Blatt,[18a] 1928; Bywater,[4] 1922). It has been claimed in several reports that simple peripapillary edema, sometimes associated with hyperemia of the nerve head, occurs in as many as 20 per cent of patients with acute recurrent attacks of malarial fever.[35] This disturbance is usually accompanied with headache and causes no significant change in vision except enlargement of the blind-spot. The same type of disturbance has been observed recently among soldiers in the tropics (Robertson,[10] 1944). The changes are said to regress ordinarily when the malaria is adequately controlled.

The vascular lesions recognized in association with malaria have also been considered to be the basis of several ocular neurologic disturbances, as well as of more general cerebral and peripheral neurologic disturbances. The ocular neurologic lesions of most significance so far as they affect vision are those of the retina and optic nerve or of the pathways of the brain. On the basis of clinical and histologic observations, it is generally believed that lesions in nerves may result from alterations in blood supply by vascular obstruction or hemorrhage in the same way that the neural elements of the retina may be affected. Disturbances of vision are recorded as a common manifestation of malaria both in recent accounts and in reports from World War I. Robertson[10] (1944) reports that a frequent complaint among troops having malaria in the southwest Pacific area was the presence of scotomas or loss of vision lasting a few minutes to several hours, followed by severe headache and persistently diminished visual acuity. There were attendant dizziness, orbital pain and tenderness with photophobia. A similar description is given by Talbot[9] (1943), who wrote that the only complaint of a large group of malarial patients from the same area was "visual disorders with heachache, often of long duration." From their experiences in World War I, Toulant[8] (1938) and Kirk[21] (1918) also reported their impressions of the frequency of reduction of vision with malaria. Changes in the optic nerve and in the fundus sufficient to account for the amblyopia and amaurosis have been described in some cases, while cerebral lesions have been considered responsible for the disturbances in others.[9] In addition to the cases of obvious disease, there is usually mentioned a considerable proportion of cases in which the disturbance of vision is ascribable only to refractive or accommodative changes.[36]

Those lesions resulting in loss of vision which are evident ophthalmoscopically are optic neuritis or atrophy of the optic nerve and degenerative or hemorrhagic lesions of the retina and choroid. In the malarial patients with visual disturbances examined by Robertson[10] (1944), atrophic retinitis, with accumulations of pigment in the choroid and optic neuritis were the changes most frequently found in the fundus. These lesions were present in 4.9 and 2 per cent, respectively, of a series of 1,000 soldiers examined for some reason other than trauma in the ophthalmic clinic of an Army station hospital in the southwest Pacific in 1943. Malarial parasites

30. (*a*) Sédan, J.: Cécité temporaire par angiospasme rétinien d'origine paludique, Ann. d'ocul. **166:** 705, 1929. (b) Lavagna, J.: Contributions à l'étude de troubles oculaires paludiques, Thesis, Faculté de Montpellier, 1920. (*c*) Raynaud, M., cited by Villard.[26a] (*d*) de Andrade.[28a]

31. Laveran: Deuxième note relatif à un nouveau parasit trouvè dans le sang des malades atteints de la fièvre, Bull. Acad. de méd. **9:**1346, 1880.

32. Fisher, J. H.: Disease of the Retina, Tr. Ophth. Soc. U. Kingdom **41:**235, 1921.

33. Dudgeon, L. S.: A Case of Malignant Malaria, Tr. Ophth. Soc. U. Kingdom **41:**237, 1921.

34. Guarnieri, G.: Ricerche sulle alterazioni della retina nella infezione acuta da malaria, Arch. per le sc. med. **21:**1, 1897.

35. Bushmich, D. G.: Ocular Symptoms in Malaria, Vestnik oftal. **17:**265, 1940. Yarr, M.: Malarial Infection of the Eye, Brit. M. J. **2:**870, 1898; Ann. d'ocul. **121:**469, 1899. Motegi and others.[28b]

36. Wood, D. J.: Accommodative Failure in Malaria and Influenza, Brit. J. Ophth. **4:**415, 1920. Robertson[10]

were present in the blood of 75 per cent of the men in the area. In a number of Robertson's patients who complained of sudden diminution of vision, atrophic retinitis or optic neuritis ultimately became apparent, although ophthalmoscopic examination disclosed no abnormalities at the onset of symptoms. In Talbot's observations on military personnel infected with malaria, optic neuritis was also noted as a cause of amblyopia, headache and a type of orbital pain that was made worse by pressure or movement of the eye.[9] The experience of these recent observers corresponds closely to that reported by many others in the past.[37] It is agreed by most authors that the optic neuritis of malaria is followed by atrophy in a relatively small proportion of cases when adequate antimalarial treatment is given.[38] Typical retrobulbar neuritis is less common than papillitis.[39] Opacities in the vitreous are rarely reported to be present with changes in the fundus associated with malaria, and iritis and cyclitis are seldom attributable to malaria except possibly for a mild iritis which occasionally accompanies herpetic keratitis. Similarly, cataract is a rare complication among the ocular disturbances of malaria.[40]

In a consideration of visual disturbances in malaria, the possibility of toxic effects from quinine in therapeutic use must be ruled out. It has generally been held that the changes associated with toxic amblyopia or amaurosis due to quinine are sufficiently typical to be distinguished from malarial manifestations.[16] Pamaquine naphthoate may also cause changes in vision, but this drug has been employed by so small a proportion of physicians reporting on ocular complications of malaria that there has been little opportunity for misinterpretation. With the current increased use of other antimalarial agents, such as quinacrine, which appear to be considerably less toxic to the eye, the possibility of confusion is, of course, reduced. An impression of a relatively low incidence of visual disturbances due to quinine itself is obtained when it is considered that although more than 200 cases of ocular manifestations have been reported in the one hundred years since the first observation of such a complication quinine has been one of the most widely used drugs during this period.[41] Consistent with a low incidence is the report that, although the use of quinine for malaria in [illegible] region of Memphis, Tenn., has been relati[illegible] common, no recent case of blindness due to [illegible] nine poisoning and only 2 cases of atrophy [illegible] the optic nerve produced by the drug w[illegible] recognized among 30,000 new patients in [illegible] ophthalmic clinics of that city during a ten y[illegible] period (1926-1936) and only 1 new case w[illegible] recorded in the general hospitals of the s[illegible] city during a five year period.[41] Similar figu[illegible] were reported by Manson[42] (1920), who fou[illegible] only 2 cases of amaurosis due to quinine pois[illegible] ing and none of amblyopia or atrophy of the op[illegible] nerve due to the drug among 12,000 patie[illegible] treated for malaria in military service in Wo[illegible] War I. However, blindness is at times p[illegible] duced by quinine and has been observed a[illegible] both minute and massive doses. Interpretatio[illegible] of the ophthalmoscopic observations with reg[illegible] to the mode of the toxic action of quinine h[illegible] been the subject of considerable controver[illegible] centering on the question whether the effect [illegible] the drug on the retina is a result of ischem[illegible] due to alterations produced in the vessels or o[illegible] direct toxic action on the neural elements the[illegible] selves. Without a detailed discussion of the e[illegible] dence, it may be said that clinical, histologic a[illegible] experimental observations have not yet been a[illegible] quate to settle the question, but recent opini[illegible] seems to favor a direct action of quinine on neu[illegible] elements of the retina as a primary factor[illegible] Clinically, the onset of amaurosis is sudden [illegible] complete to the extent of loss of light percepti[illegible] In most instances the pupils have been describ[illegible] as dilated and fixed. Examination of the fund[illegible] at first reveals only edema of the whole reti[illegible] with a red macula, but in the course of a we[illegible] or two the disks become pale and the arteries m[illegible] become greatly narrowed. During this period [illegible] apparent advance in the pathologic process [illegible] the fundus, vision often gradually returns. T[illegible] coincidence of these phenomena has been refer[illegible] to as the "paradox of quinine amaurosis."[44] [illegible] some cases, however, vascular and visual chang[illegible] did not coincide, while in a few cases no arter[illegible] narrowing was observed.[45] In subsequent mont[illegible]

37. Woods, H.: Optic Neuritis After Measles and Intermittent Fever, Arch. Ophth. **21**:95, 1892. MacNamara: Malarial Neuritis and Neuro-Retinitis, Brit. M. J. **1**:540, 1890. Sulzer.[2]

38. Toulant.[8] Kiep.[16] Blatt.[18a]

39. Villard.[26a] Toulant.[8]

40. Blatt.[18a] Dedimos.[5]

41. Richardson, S.: The Toxic Effect of Quinine on the Eye, South. M. J. **29**:1156, 1936.

42. Manson, W. H.: Personal Experiences on [illegible] Ocular Sequelae of Malaria, Glasgow M. J. **93**:[illegible] 1920.

43. McGregor, I. S., and Loewenstein, A.: Quin[illegible] Blindness, Lancet **2**:566, 1944.

44. Duggan, J. N., and Nanavati, B. P.: Quin[illegible] Amblyopia, Brit. J. Ophth. **15**:160 and 164, 1931.

45. Pelner, L., and Saskin, E.: Toxic Amaur[illegible] Due to Quinine: Treatment with Sodium Nitrite A[illegible] ministered Intravenously, J. A. M. A. **119**:1175 (A[illegible] 8) 1942. Ballantyne, A. J.: Quinine Amaurosis w[illegible] Report of a Case, Brit. J. Ophth. **1**:153, 1917. F[illegible] L. W.: Acute Uni-Ocular Neuritis, Am. J. Op[illegible] **1**:113, 1884. Duggan and Nanavati.[44]

ntral color scotomas may be present for a time, t progressive improvement in central vision is ually noted, almost always with persistent con- ntric constriction of the fields and hemeralopia. haracteristically, at the relatively late stage, the tic disks are white and the retinal vessels much duced in diameter. In occasional cases loss of sion is permanent.[43] The clinical features of inine poisoning thus differ in several respects om the changes attributed to malaria, especially ith regard to the extent of the retinal edema and scular alterations, as well as to the character the visual loss.

The occurrence with malaria of neurologic sturbances other than those concerned with sion has been repeatedly described, both re- ntly and in the past. Among soldiers hospital- ed for malaria in World War II, "neuralgia" hyperalgesia of various sensory nerves has en described as having a high incidence (18 er cent) by Harvey[46] (1944). In most cases e malaria was caused by Plasmodium vivax. he neurologic disturbances are explained by arvey as probably due to transient lowering of e threshold of excitability of nerves which are bjected to asphyxia from partial blocking of eir blood supply. The symptoms noted are ain or burning and tingling of varying duration the distribution of a single cranial or peripheral erve, occurring most commonly in the first week ter the onset of active malaria, during or just rior to the first acute attack of fever. Symptoms lso occur often, but with diminishing frequency, subsequent attacks, as well as during latent eriods. Numerous authors have noted the fre- ent occurrence with malaria of neuralgia of e trigeminal nerve, especially of the supra- rbital and infraorbital branches of the ophthal- ic division.[47] This complication was observed y Griesinger[48] in 13 of 414 cases of malaria, hile it was said to be one of the most frequent omplications of benign tertian malaria by Tou- nt[8] and of masked malaria by Bispham.[11a] Most characteristically, pain, localized in the dis- ribution of the supraorbital nerve, starts rapid- y at the beginning of a chill and lasts from two o five hours. Often the pain is succeeded by yperesthesia in the same location but may be ecurrent with subsequent attacks of fever or be eplaced with hypesthesia. Usually the neuralgia ay be controlled by antimalarial treatment.[8]

The attack of hyperalgesia is often accompanied with conjunctival hyperemia, tearing and photophobia and may be followed by the appearance of herpetic keratitis with corneal hypesthesia. Consideration of the neurotropic characteristics of the herpes virus and the occurrence of herpetic lesions following other types of disturbances of the trigeminal nerve, such as those produced by operative procedures[49] or a toxic agent,[50] has suggested to some observers a possible causal relationship between the malarial trigeminal neuralgia and herpetic keratitis.[18a]

Relatively infrequently, transient ocular motor disturbances, seldom with permanent paralysis,[8] have been ascribed to malaria. Paresis of the abducens nerve has been noted more commonly than weakness of the other ocular muscles.[51] Less often, facial paralysis with lagophthalmos has been reported.[16] It has been suggested that the mechanism producing the paresis may be an injury of the motor nerves as a result of vascular changes. A similar mechanism has been postulated for motor disturbances of the extremities associated with malaria, which differ, however, in that they are characterized by increased muscular tone accompanied with hyperalgesia (Harvey,[46] 1944). It has been suggested by Blatt[18a] (1928) that the ocular motor disturbances may be the result of central lesions, since their onset is often associated with headache and dizziness. Involvement of isolated muscles would be consistent with nuclear lesions, but the usual transitory nature of the paresis might be better explained by peripheral disturbances. Attempts to account for the muscular weakness on a toxic basis have not explained how isolated muscles may be involved without disturbances of the other muscles.

Besides the various ocular manifestations usually described, there are less well recognized changes which warrant brief mention. Among these are the "malarial vessels" of Goldfeder,[52] which are described as large, superficial conjunctival vessels running horizontally without branching until they reach the limbus, and which Goldfeder claimed to be pathognomonic of malaria. Similar vessels have been observed in a

46. Harvey, A. M.: A Type of Neuritis Associated with Malarial Fever, Bull. Johns Hopkins Hosp. **75:** 25, 1944.

47. Santos Fernandez, F., and Madan, D.: Les hématozoaires de Laveran dans la névralgia ophtalmique, Arch. d'opht. **12:**266, 1892. Carlotti.[6] Kiep.[16]

48. Griesinger, cited by Toulant.[8]

49. Richter, R. B.: Observations Bearing on the Presence of Latent Herpes Simplex Virus in the Human Gasserian Ganglion, J. Nerv. & Ment. Dis. **99:**356, 1944.

50. Humphrey, J. H., and McClelland, M.: Cranial Nerve Palsies with Herpes Following General Anesthesia, Brit. M. J. **1:**315, 1944.

51. Blatt.[18a] Kirk.[21]

52. Goldfeder, A. E.: Malaria und Auge: Ueber ein allgemein zugängliches Augensymptom der chronischen und larvierten Malaria, Arch. f. Schiffs- u. Tropen-Hyg. **40:**207, 1936.

large proportion of patients with malaria by Rozende,[53] Mufel [54] and Bushmich,[35] but these vessels were also found in patients with diseases other than malaria.[35] Goldfeder and associates [55] also described the occurrence of "blue stripes" in the fundus as a characteristic of malaria, but it is uncertain whether this lesion corresponds to changes described by other observers. Inequality of the pupils, attributed to unilateral irritation of the sympathetic nervous system, was observed by Dedimos [5] in 25 per cent of malarial patients with moderate splenic enlargement, and this observation has not been seriously at variance with the reports of other authors.[35] An icteric tinge of the conjunctiva has often been described in cases of malaria, even of the masked type.[56] This discoloration is considered to be due to deposition of malarial pigment and is analogous to the discoloration of the nerve head and ret observed with chronic malaria. There appear be no characteristic conjunctivitis or scler associated with malaria.[57]

In conclusion, it appears that malaria may the inciter of several characteristic disturban in various parts of the eye. The processes countered are mostly monocular but moderat incapacitating, including the relatively freque though nonspecific, complication of herpetic ker titis and several of the disturbances which app to be best explained on the basis of vascu lesions attributable to the malarial parasi Lesions of the choroid, retina and optic ner which from histologic evidence appear to be d to emboli of parasitized cells and which are co monly bilateral, appear to be the most serious the complications, because of their interfere with vision. Treatment of these ocular dist bances with antimalarial drugs has in gene been successful, except in case of the herpe keratitis, caused by a virus, for which spec chemotherapy is lacking.

243 Charles Street.

53. Rozende, C.: Contributo brasileira ao signal ocular de Goldfeder, no diagnostico da malaria chronica e larvada, Cong. argent. de oftal. (1936) **2**:626, 1938.

54. Mufel (1936), cited by Bushmich.[35]

55. Goldfeder, A. E., and Moldavskaja, V. D.: Malaria and the Eye, Arch. Ophth. **17**:228 (Feb.) 1937.

56. Fialho.[7] Talbot.[9] Manson.[42]

57. Dedimos.[5] Carlotti.[6]

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Ophthalmologic Seminar, Emory University School of Medicine.—Emory University School of Medicine will hold an ophthalmologic seminar honoring the memory of Dr. Abner Wellborn Calhoun on April 4 to 6, 1946. Guest lecturers will be Dr. William Benedict, Dr. John Dunnington, Dr. Parker Heath, Dr. Walter Lillie, Jr. Derrick Vail and Dr. Frank Walsh. All members of the ophthalmologic profession are cordially invited as guests of Emory University. Reservations at the Atlanta Biltmore Hotel should be made early.

The Scientific Exhibit, Ninety-Sixth Annual Session of the American Medical Association.—Application blanks are now available for space in the Scientific Exhibit at the Ninety-Sixth Annual Session of the American Medical Association, to be held at San Francisco, July 1 to 5, 1946. Applications for space will close on February 25.

Requests may be sent either to Dr. Georgiana Theobald, 120 Medical Arts Building, 715 Lake Street, Oak Park, Ill., who is the representative to the Scientific Exhibit from the Section on Ophthalmology, or to the Director, the Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10.

Refresher Course in Ophthalmology, Washington University School of Medicine.—Washington University School of Medicine, in St. Louis, announces a four week intensive refresher course in ophthalmology from June 3 through June 29, 1946. The 131 hours of didactic lectures will cover the important phases of ophthalmology. The course is designed primarily for the returning veteran but should also serve as an excellent review for candidates for the examination by the American Board of Ophthalmology. Tuition fee: $200. An outline of the course, as well as more detailed information, will be sent on request. All applications or inquiries should be addressed to Dr. Richard G. Scobee, director of graduate training in ophthalmology, Washington University School of Medicine, 640 South Kingshighway Boulevard, St. Louis 10.

UNIVERSITY NEWS

The William F. Norris and G. E. de Schweinitz Chair of Ophthalmology.—The William F. Norris and G. E. de Schweinitz Chair of Ophthalmology was established in the University of Pennsylvania on June 28, 1945, by a bequest under the will of Dr. George E. de Schweinitz, professor of ophthalmology in the University of Pennsylvania School of Medicine from 1901 to 1924, and at one time a trustee of the university. The income of a fund of $150,000 is available for the maintenance of the chair.

Dr. Francis Heed Adler is the present incumbent of the chair.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

ABERRANT OPTIC NERVE FIBRES FOUND BETWEEN RETINA AND HEXAGONAL CELLS. A. LOEWENSTEIN, Brit. J. Ophth. **29:** 180 (April) 1945.

Two cases of aberrant nerve fibers of the optic nerve of different sizes are described. The first type was found in a case of pigmented tumor of the optic disk infiltrating the neighboring retina and choroid. The lesion is assumed to be a malignant degeneration of a pigmented nevus of the optic disk. This type involves maldevelopment of the posterior retinal layers in front of the growth. The second type was seen in a case of hypertensive retinopathy with edematous swelling of the papilla and a large druse. The nerve fiber tissue found between the retina and the pigmented epithelium was degenerated in a ganglioform manner. The retina in front of this tissue was well developed. A mechanical pushing out of the optic nerve fibers, due to the edema and the pressure of the druse, is assumed to be the cause.

The article is illustrated.

W. ZENTMAYER.

Injuries

TRAUMATIC OCULAR INJURIES IN SOLDIERS. B. RONES and H. C. WILDER, Am. J. Ophth. **28:** 112 (Oct.) 1945.

This is a statistical study of 399 enucleated eyes received at the Army Institute of Pathology. Analysis, interpretation and clinical correlation will be attempted in studies now under way. The authors call attention to the absence of sympathetic ophthalmia.

W. S. REESE.

IMPROVED TREATMENT FOR CHEMICAL BURNS OF THE EYE. L. W. OAKS, Am. J. Ophth. **28:** 370 (April) 1945.

Oaks believes it likely that chemicals may enter the anterior chamber in burns of the eye. He believes that paracentesis of the cornea should be established as a standard procedure in every case of a moderate or severe burn of the cornea in which any destruction of tissue or haziness results, irrespective of the chemical involved.

W. ZENTMAYER.

INTRAOCULAR FOREIGN BODIES. W. O. LODGE, Brit. J. Ophth. **29:** 205 (April) 1945.

Lodge describes a technic for the localization of intraocular foreign bodies in cases in which the vision of the injured eye is good but the foreign body is located too far forward to be seen with the ophthalmoscope.

An illustrative case is described.

W. ZENTMAYER.

Lens

ELECTRICAL CATARACT: NOTES ON A CASE AND A REVIEW OF THE LITERATURE. A. L. ... and M. KLEIN, Brit. J. Ophth. **29:** ... (April) 1945.

A man aged 51 came into contact with ... electrical apparatus. A discharge at 11,000 ... passed by sparking contact with his metal-rim... glasses and ear pieces. Second and third deg... burns were present around the orbits and al... the temples and the bridge of the nose. Th... were second and third degree burns of the up... part of the body. Visual symptoms develo... six months after the accident when the si... began to fail. There was no pathologic cha... except in the lenses. Both lenses showed op... ties, chiefly vacuoles in the anterior capsule a... subcapsular grayish dots, in some places c... fluent. On the anterior capsule of the left l... was a seal-like gray opacity. Corrected vis... was 6/12 in each eye; at the end of sixte... months the ocular condition remained unchang...

A review of the literature shows that the nu... ber of cataracts due to contact with an elec... current has increased recently, corresponding ... the increase in the number of electrical accid... of all kinds. The onset of the ocular disturba... is usually delayed. There is not sufficient e... dence to state the cause of this type of cataract ... the process by which it develops.

As a practical suggestion, it is advisable t... persons employed in electric power stati... should not wear spectacle rims containing me...

The article is illustrated.

W. ZENTMAYER.

THE EFFECT OF ASCORBIC ACID ON THE OCCURRENCE OF HYPHEMIA AFTER CATARACT EXTRACTION. I. MANN and A. PIRIE, Br... J. Ophth. **29:** 175 (April) 1945.

The results of all cataract operations in t... hospital for 1942-1943, when ascorbic acid w... not given, were compared with a similar series ... 1943-1944, with the difference that in the s... ond series an attempt was made to saturate ev... patient with ascorbic acid at the time of ope...

on. All other factors, such as surgeons, type of operation and diet in hospital, remained the same throughout the two years.

The authors conclude that there is no evidence that the occurrence of hyphemia following cataract extraction is influenced by administration of ascorbic acid.

W. ZENTMAYER.

Lids

ACQUIRED BLEPHAROPTOSIS. E. B. SPAETH, Am. J. Ophth. **28:** 1073 (Oct.) 1945.

A brief classification is presented for convenience in consideration of the various forms of acquired ptosis of the upper lid. The surgical needs for the correction of these defects are varied and exacting. Suggestions for the maximum correction of these dissimilar situations are presented. Since the procedures outlined have proved satisfactory in many instances. Recognized indications demand varied methods of correction. One surgical technic will best correct only one type of the condition. Attention to this exacting situation should give excellent results; its neglect will bring disappointment.

Spaeth presents a number of photographs and descriptions.

W. S. REESE.

Neurology

ELECTRICAL SENSITIVITY OF THE EYE IN SOME OPTIC-NERVE DISEASES RESULTING FROM CRANIO-CEREBRAL TRAUMATA. S. V. KRAVKOV and A. N. MURSIN, Am. J. Ophth. **28:** 363 (April) 1945.

Kravkov and Mursin feel that the electrical sensitivity of the eye might help in differentiating optic neuritis and choked disk, and from their investigations they conclude that determination of this factor is helpful and frequently reveals abnormalities when the ophthalmoscopic examination does not.

W. S. REESE.

WERNICKE'S DISEASE (ENCEPHALITIS HEMORRHAGICA SUPERIORIS). D. KRAVITZ and R. H. STOCKFISCH, Am. J. Ophth. **28:** 596 (June) 1945.

Three cases of superior hemorrhagic encephalitis are reported in which there was no history of alcoholism but the condition was due to dietary deficiency.

A complete cure was obtained in the second and third cases and an almost complete cure in the first case. In case 1 the disease had been present for a much longer time, and the symptoms were much more severe and had reached the irreversible stage but, fortunately, to only a slight extent. It is interesting to note that only in case 3 were other features of vitamin B deficiency present, namely, cheilosis and glossitis.

W. S. REESE.

PHOTIC DRIVING. A. WALKER, J. WOOLF, W. HALSTEAD and T. CASE, Arch. Neurol. & Psychiat. **52:** 117 (Aug.) 1944.

Early in the study of the electrical activity of the cerebral cortex Berger noted that a photic stimulus to the retina notably altered the spontaneous alpha rhythm. This observation gave added impetus to the study of the phenomena associated with stimulation of the visual system, which led to the discovery of one of the most interesting methods of modulating the pattern of the occipital electroencephalogram, namely, that of intermittent photic stimulation of the retina, or "photic driving." The modifications of the normal cortical rhythms which may be produced by this method permit certain analyses of normal, and possibly pathologic, visual mechanisms.

The authors found that intermittent photic stimulation of the retina of the cat, dog, monkey and man may modify the electroencephalogram from the occipital cortex to take on a frequency synchronous with that of the flicker. The effect is augmented by increasing the intensity of the luminous flux, with a maximum at approximately 80 foot candles. The driving is more pronounced when the photic stimulus is at the blue end of the spectrum than when it is at the red end. The cortex of the macaque monkey may be made to follow a flicker with a frequency of 34 per second, but the optic nerve and the lateral geniculate body will follow frequencies of 62 and 59 cycles per second, respectively. Lesions of the visual pathways impair photic driving.

R. IRVINE.

WERNICKE'S DISEASE: CLINICAL AND PATHOLOGIC STUDY OF 42 CASES. H. E. RIGGS AND R. S. BOLES, Quart. J. Stud. on Alcohol **5:** 361 (Dec.) 1944

Riggs and Boles present a study of 42 cases in which the diagnosis of Wernicke's disease (superior hemorrhagic polioencephalitis) was confirmed by necropsy. A history suggesting chronic alcoholism was obtained in only 18 cases, while in all the cases there were either clinical signs of a deficiency state or, at necropsy, evidence of organic change which would contribute to the condition. The diagnosis in these 42 cases was made almost invariably at necropsy on the basis of characteristic changes in the brain. The clinical syndrome described by Wernicke was found to be of little value as a criterion of diagnosis. Disturbance of psychic function was present in all cases, usually as an initiating symptom, and in 70 per cent it was associated with other signs of involvement of the nervous system. The classic triad of clouding of consciousness, ophthalmoplegia and ataxia was not noted in its entirety in a single case. The clinical and necropsy observations in 42 cases of Wernicke's disease suggest that in these cases nutritional

deficiency provided the essential background for the condition. Alcohol, although contributing to the deficiency state in at least 43 per cent of the series, was apparently not a primary factor in the genesis of the disease.

J. A. M. A. (W. ZENTMAYER.)

Ocular Muscles

CAUSES OF FAILURE IN THE TREATMENT OF SQUINT. F. D. COSTENBADER, Am. J. Ophth. **28:** 1123 (Oct.) 1945.

After a somewhat brief reference to the literature, the pitfalls in the treatment of squint are listed and discussed. The commonest and most important factors in failure to correct the defect would seem to be (1) persisting amblyopia, due to belated, inconstant or insufficient occlusion; (2) failure to recognize or sufficiently to treat suppression and/or abnormal retinal correspondence; (3) difficulty in managing a combined vertical and lateral imbalance; (4) failure to distinguish between the accommodative and the mechanical elements in a given case of squint, and (5) failure to stabilize and obtain functional cure by adequate postoperative orthoptic training.

W. S. REESE.

AN ANALYSIS OF ONE HUNDRED CASES OF STRABISMUS TREATED ORTHOPTICALLY. R. U. GILLAN, Brit. J. Ophth. **29:** 420 (Aug.) 1945.

The purpose of the survey was a desire to ascertain at first hand the effects of orthoptic treatment in developing (1) orthopsis and (2) stereopsis.

Analysis of 63 cases in which orthoptic treatment only was given revealed that in 36 cases the eyes became straight, or nearly straight, and good stereoscopic vision developed. The conclusion is reached that a prerequisite to successful treatment by orthoptic means only is the existence of simultaneous perception and fusion and strabismus of not more than 25 degrees, preferably much less, viz.: about 10 degrees.

Analysis of 37 cases in which combined orthoptic treatment and operation was employed showed that the eyes became straight, or nearly straight, in 23 cases and good or fair stereoscopic vision developed in 17 cases. The conclusion is reached that good stereoscopic vision is an important factor in maintaining orthopsis even when operation has been performed.

An analysis is made of a control series of 50 cases in which the patients were under observation for an average of nine months and had no treatment except the prescription of glasses. In none of these cases did orthopsis or stereoscopic vision develop.

An analysis is made of the results of refraction in the 100 cases under review and of the effects of correction with glasses at the commencem of orthoptic treatment. In only 3 cases were eyes straight at the beginning of treatment; 25 cases there was reduction of squint, and in cases there was no change in the degree of squi The conclusion is reached that the lower degr of squint are most likely to be corrected w glasses but that an essential condition of t eventuality is the preexistence of simultane perception and fusion and a capacity for devel ment of good stereoscopic vision; that not e under such conditions do all eyes become strai but that with the addition of orthoptic treatm they are very likely to do so.

In the light of these results, the possible ca of strabismus is discussed, and the conclusion reached that the absence or failure of stereosco vision is the main etiologic factor in the produ tion of concomitant strabismus.

Some objections to this theory are discuss but they are not thought to invalidate it.

W. ZENTMAYER.

Orbit, Eyeball and Accessory Sinuses

ACTINOMYCOSIS OF THE ORBIT. E. CHAN, C nese M. J. **63:** 98 (Jan.) 1945.

A Chinese merchant aged 58 had a history a nodule developing in the right lower lid f five years. There was an ulcerating mass a herent to the inferior orbital margin with a sin leading into the orbit, which discharged a gray yellow fluid. The discharge contained knots myceliums with radially projecting tips—a tinomycetes. Tissue from the mass was made of inflammatory and epithelioid cells and ma giant cells of the foreign body and Langerha type.

W. ZENTMAYER.

Parasites

THELAZIASIS OF THE CONJUNCTIVA. S. LIANG, Chinese M. J. **63:** 70 (Jan.) 1945.

A case of infection of the conjunctiva wi Thelazia callipeda is reported from Kweiyan Kweichow. Unlike previously reported case there was no complaint of subjective symptoms i the infected eye. The parasites were accidentall discovered during routine examination. Thel ziasis, like other parasitic diseases, produce eosinocytosis. The source of infection in th case was probably dogs or cats.

W. ZENTMAYER.

Physiologic Optics

DIRECT UTILIZATION OF THE EYE AS A CAMER W. A. MANN, Am. J. Ophth. **28:** 451 (May 1945.

Mann describes experiments on animal eye demonstrating that the eye can be used as camera by putting a film behind an optical gla placed over a window cut in the region of th

macula, the glass being of a curvature approximating the posterior conformity of the globe.

W. S. REESE.

Retina and Optic Nerve

DRUSEN (HYALINE BODIES OF THE OPTIC DISK). H. P. WAGENER, Am. J. M. Sc. **210:** 262 (Aug.) 1945.

Wagener makes a critical review of the literature of drusen and gives the results of electroencephalographic studies on 6 patients with drusen in the optic disks. The results are interesting though probably not clinically significant. The records of 2 patients were essentially normal; the electroencephalogram of 1 patient showed slight delta activity in the right temporal area. A third patient, who presented a posttraumatic syndrome resulting from a head injury, had a record of low potential but otherwise normal. The record of the fourth patient showed some dysrhythmia; that of the fifth patient, dysrhythmia and bilateral occipital delta activity, grade 1 and 2, and that of the sixth patient, generalized dysrhythmia. All the patients except the sixth had normal roentgengrams of the head. In the sixth patient the sella was enlarged and the dorsum eroded. One of the patients presented Adie's syndrome; 1 had syphilis of the central nervous system, and the sixth had, with emotional instability, signs of an organic cerebral disorder, mainly in the cerebellum.

Although it cannot be considered definitely proved at present that drusen of the optic disk are really slow-growing astroblastomas of hereditary and familial occurrence and that they represent a variant of tuberous sclerosis, the evidence presented is at least suggestive and intriguing and warrants further study and investigation.

W. ZENTMAYER.

CHANGES AT THE MACULA DUE TO SOLAR RADIATION. C. MCCULLOCH, Am. J. Ophth. **28:** 1115 (Oct.) 1945.

Seven cases of residual change at the macula probably due to solar radiation are reported. A method for plotting very small central scotomas with the tangent screen and a method for noting the properties of the normal macular reflex are described.

A small central scotoma was found in 6 of the 7 cases. The fundi in all 7 cases showed an abnormal yellow spot at the macula, surrounded by a dark ring. In 6 of the 7 cases the lesion was in the right eye. In 4 of these 6 cases the right eye was dominant; in 1 case the left eye was dominant, and in 1 case the dominance was not recorded.

In the discussion, it is pointed out (1) that other causes for cyst at the macula must be considered and the condition differentiated from tobacco-alcohol amblyopia, colloid excrescences and the areas of suppression seen in scotometric examinations, and (2) that the pathologic change at the macula probably centers at the level of the pigment epithelium and not at the level of the retina.

W. S. REESE.

Uvea

ANGIOID STREAKS OF THE DEEP LAYERS OF THE RETINA. A. J. BEDELL, Am. J. Ophth. **28:** 601 (June) 1945.

Bedell records observations made on angioid streaks during the past several years, with special reference to the study of 4 cases. One of the patients was under observation for a short time, the second for four years, the third for eight years and the fourth for fourteen years. The author states that the narrow circumpapillary atrophy as such has nothing to do with the streaks and that, furthermore, when degenerative lesions of the macula develop they follow the usual clinical course of deep retinal or superficial choroidal hemorrhages, with exudate, edema and an expanding ring of blood. After many months, recurring hemorrhages stop; the exudate becomes organized, and the scar persists throughout life. This is not conceived to be an integral part of angioid streaks. The author does not believe that the ruptures on Bruch's membrane and the accompanying pseudo xanthoma elasticum are part of the same process, certainly not in all cases.

The article is illustrated.

W. ZENTMAYER.

DIABETIC IRIDOPATHY. C. A. CLAPP, Am. J. Ophth. **28:** 617 (June) 1945.

Clapp reports 2 cases of this condition.

The term iridopathy is to be used when there occur changes in the iris which are of metabolic, not inflammatory, origin.

Diabetes may cause changes in the iris which may be confused with malignant melanoma.

Clinical and pathologic observations have apparently been confirmed by animal experimentation.

A further study of theses changes is desirable, especially to ascertain whether they are limited chiefly to the diabetic patient, and to determine the cause.

W. S. REESE.

Sympathetic Ophthalmia

SYMPATHETIC OPHTHALMIA FOLLOWING SUBCONJUNCTIVAL RUPTURE OF THE EYEBALL. C. A. PERERA, Am. J. Ophth. **28:** 581 (June) 1945.

Perera reviews sympathetic ophthalmia, especially that following subconjunctival rupture of the globe. He reports a case of the latter and con-

cludes that allergy to uveal tissue plays an etiologic role in the production of sympathetic ophthalmia.

W. S. REESE.

Therapeutics

THE EFFECT OF DETERGENT ON THE PENETRATION OF SODIUM SULPHACETAMIDE (ALBUCID SOLUBLE) INTO OCULAR TISSUES. M. GINSBURG and J. M. ROBSON, Brit. J. Ophth. **29:** 185 (April) 1945.

The penetration of sodium sulfacetamide into the ocular tissues was studied both in living rabbits and in isolated ocular tissues. The application of the drug with a wetting agent, Duponol ME dry, increases the penetration of sodi sulfacetamide into and through the cornea. R moval of the corneal epithelium results in great increase in the penetration of the sulfo amide drug into and through the cornea; that the epithelium acts as a barrier to the pass of the drug. The wetting agent does not increa the passage of the drug into the denuded corn (i. e., the cornea with the epithelium removed It may be concluded that the wetting agent ac by overcoming the epithelial barrier. The resu suggest that addition of a wetting agent to sodiu sulfacetamide is of most value with infections the cornea and iris.

W. ZENTMAYER.

Society Transactions

EDITED BY W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

RUDOLF AEBLI, M.D., *Chairman*

TRUMAN L. BOYES, M.D., *Secretary*

Regular Meeting, Nov. 19, 1945

Present Status of Radiation Therapy of Ocular Diseases. DR. HAYES MARTIN.

Dr. Martin discussed the forms of radiation therapy which have been used at the Memorial Hospital in the treatment of lesions about the eye. These consist of roentgen radiation, the unfiltered radon bulb and radon gold seeds. He pointed out that filtered radium applicators should never be used about the eye because of the impossibility of providing adequate protective shielding with the applicator. He discussed the various complications and untoward sequelae of radiation therapy about the eye and pointed out that many of these complications can be avoided by use of the proper technic; others, although not completely preventable, are often justifiably incurred provided that the disease for which the treatment is given is more serious than the complication. Radiation therapy about the eye is indicated for only a limited number of malignant tumors, benign neoplasms and diseases. He briefly discussed the technics of irradiation and the dosage and showed a number of illustrative cases.

Exophthalmos Caused by Eosinophilic Granuloma of Bone. DR. MAYNARD WHEELER.

Eosinophilic granuloma of bone was first recognized as a distinct entity in 1940. At least 37 cases have now been reported, but in only 1 was exophthalmos present. The tumor occurs as a rapidly developing, painful swelling over the skull, a rib or a long bone in a child or a young adult. Multiple lesions are frequently shown roentgenographically. The diagnosis is made by the finding on histologic examination of large numbers of histiocytes, many giving evidence of phagocytic activity, and occasional large multinuclear giant cells; numerous eosinophilic and neutrophilic leukocytes, and many clumps of mononuclear eosinophilic cells.

A typical case was reported in a man aged 34 who complained of exophthalmos with pain of five weeks' duration. The lesion was curetted, with recovery. This favorable result has been reported in all cases whether excision, curettage or roentgen irradiation was employed.

Dermatomyositis with Retinopathy. DR. JACK V. LISMAN.

This paper will be published in full, with discussion, in a future issue of the ARCHIVES.

Uses of Air in Ophthalmology. DR. WENDELL L. HUGHES, Hempstead, N. Y.

This paper will be published in full, with discussion, in a future issue of the ARCHIVES.

Ocular Changes Associated with the Blood Dyscrasias. DR. ISAAC S. TASSMAN, Philadelphia (by invitation).

This paper will be published in full, with discussion, in a future issue of the ARCHIVES.

Book Reviews

New Goals for Old Age. Edited by George Lawton, D.Sc. Price, $2.75. Pp. 210. New York: Columbia University Press.

Much water has flowed under the bridges of social and cultural theory since a famous physician notified all and sundry, in a more or less strabismic world, that every man of 40 was, not, as Stevenson claimed, either a physician or a fool but definitely *passé* for effective thought or activity. Today one notes as an indication of progressive civilization a similarly advancing preoccupation with the physical and spiritual problems of the very young and the very old. *Les extrèmes se touchent* in a way which probably did not occur to the French commentator, and infancy as well as senility—*sit venia verbo*—especially the latter, is of interest to a large reading public of laymen, as well as physicians.

It was Stevenson, again, who said "Age cannot bring, it must find, the philosophic mind," and those who seek for this *pium desiderium,* a consummation devoutly to be wished, will find much of interest in this symposium, with a wealth of information from practical experience and wide study, as well as humor and wit. The editor contributes largely to this harvest in his prologue to what he calls a conspirational collection of papers. These, numbering nearly a score, range over the broad field of physical, mental and spiritual reactions of presenescence. The result is an authoritatively presented, and often interestingly embellished, panorama. There are chapters on "Adjustment over the Life Span"; "Aging Mental Abilities, and Their Preservation"; "The Older Person in the Family, in the Changing Social Scene and in the World"; "Physical Changes in Old Age and Their Effects on Mental Attitudes"; "Occupational Therapy"; "The Creative Urge in Older People"; "Mental Diseases of the Aged," and an especially stimulating contribution by Alice I. Bryan, of Columbia University, School of Library Service, "Toward a Science of Bibliotherapy." The volume certainly invites one into one of the highways and byways of medicine, if not of ophthalmology, and as such will no doubt be favorably received.

An extensive bibliography and a detailed index add to its value.

PERCY FRIDENBERG

Le penicilina y sus aplicaciones en oftalmología. By Antonio Ros, M.D. Price, $3. Pp. [illegible]. México, D. F.: S. A. Bajèl, 1945.

This small book cites the importance of the new drug in clinical work and then gives a short and rather fanciful sketch of Alexander Fleming's early life.

There follows an account of his discovery and the application of the drug, its effects, toxicity and dosage. Its applications in ophthalmology are reported, and the author's method, preferably by intramuscular injection, is submitted, he preferring that means to use of collyriums or ointments and reporting cases that cured. He concludes that the drug is a prophylactic against ocular infection before operations.

The author recommends in 2 cc. the intramuscular injection of 20,000 units every three hours. The remedy has been tried by the author in treatment of various infections and of conditions in which the cause was obscure. He thinks that the treatment is particularly of value before operations, when he recommends that three injections be given, one at the time of operation and the others directly after. This remedy, in the author's opinion, is superior to the sulfonamide drugs. A bibliography is appended.

J. I. MIDDLETON

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

Faculty of Ophthalmologists

President: Brig. Sir Stewart Duke-Elder, 63 Harley St., London, W. 1, England.
Secretary: Mr. Frank W. Law, 45 Lincoln's Inn Fields, London, W. C. 2., England.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. John Foster, 45 Park Sq., Leeds.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. J. Ringland Anderson, Astor House, 108 Collins St., Melbourne, Victoria.
Secretary: Dr. D. A. Williams, 27 Commonwealth St., Sydney.
Place: Melbourne. Time: Oct. 20-26, 1946.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secetary, Dr. Mohammed Khalil.

Ophthalmological Society of Hospital de Nuestra Señora de la Luz

Chairman: Dr. Manuel J. Icaza y Dublán, México, D. F., Mexico.
Secretary: Dr. Jorge Meyrán, México, D. F., Mexico.

Ophthalmological Society of South Africa

President: Dr. A. W. Sichel, National Mutual Bldg., Church Square, Cape Town.
Secretary: Dr. J. K. de Kock, Groote Kerk Bldg., 32 Parliament St., Cape Town.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 4-6, 1946.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

São Paulo Society of Ophthalmology

President: Silvio de Almeida Toledo, Barão de Ilapetininga St., 88, 5º Andar, São Paulo, Brazil.
Secretary: Dr. Plinio de Toledo Piza, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Scottish Ophthalmological Club

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Sociedade Brasileira de Oftalmologia

President: Dr. Caldas Brito, Largo da Carioca 5-6º andar, Rio de Janeiro.
Secretary: Dr. Evaldo Campos, R. Rodrigo Silva 7-1º andar, Rio de Janeiro.

Sociedad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Arturo Etchemendigaray, Villa Constitución, Santa Fé.
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

Sociedade de Oftalmología del Norte

President: Dr. Alberto Cárdenas.
Secretary: Dr. Jorge Luis Castillo, Mendoza 421, Tucumán, Argentina.

Sociedade de Oftalmologia de Minas Geraes

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1[illegible], Bello Horizonte, Minas Geraes, Brazil.

Sociedade de Oftalmologia e Otorrinolaringologia de Rio Grande do Sul

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

Sociedade de Ophthalmologia e Oto-Rhino-Laryngologia da Bahia

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

Società Oftalmologica Italiana

President: Prof. Dott. Giuseppe Ovio, Ophthalmologic Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 1, III tr., Stockholm, Sö.

Tel Aviv Ophthalmological Society

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: San Francisco. Time: July 1-5, 1946.

American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.

American Ophthalmological Society

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 12 Clinton St., Watertown, N. Y.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Walter W. Wright, 170 St. George St., Toronto 5.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Watson Gailey, 1000 N. Main St., Bloomington, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Theodore L. Terry, 140 Marlborough St., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Julius A. Weber, 640 Stimson Bldg., Seattle 1, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1, Wash.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE and THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnstown, Pa.
Secretary-Treasurer: Dr. J. McClure, Tyson, Deposit Nat'l Bank Bldg., Dubois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val. H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Medical Society of the State of Pennsylvania, Section on Eye, Ear, Nose and Throat Diseases

Chairman: Dr. Karl M. Houser, 2035 Delancey St., Philadelphia 3.
Secretary: Dr. William T. Hunt Jr., 1205 Spruce St., Philadelphia 7.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Edmond L. Cooper, 1553 Woodward Ave., Detroit 26.
Secretary: Dr. Ralph H. Gilbert, 110 Fulton St. E., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Karl C. Wold, 1051 Lowry Bldg., St. Paul 2.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul 2.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N. St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. George P. Meyer, 410 Haddon Ave., Camden.
Secretary: Dr. John P. Brennan, 429 Cooper St., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Harold M. U'Ren, 624 Medical Arts Bldg., Portland 5.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Pennsylvania Academy of Ophthalmology and Otolaryngology

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. E. B. Fairbanks, 315 Medical Arts Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Dean Spear, 516 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn 11.
Secretary-Treasurer: Dr. Louis Freimark, 256 Rochester Ave., Brooklyn 13.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. William H. Howard, 389 Linwood Ave., Buffalo 9.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo 9.
Time: Second Thursday of each month from October to May.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Samuel J. Meyer, 58 E. Washington St., Chicago 2.
Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.
Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. M. Paul Motto, Rose Bldg., Cleveland.
Secretary: Dr. H. H. Wygand, Guardian Bldg., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. Erwin W. Troutman, 21 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. T. Rees Williams, 380 E. Town St., Columbus 15, Ohio.
Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.
Time: 6:30 p. m., third Tuesday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.
Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Wesley G. Reid, 667 Fisher Bldg., Detroit 2.
Place: Club rooms of Wayne County Medical Society.
Time: First Monday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.
Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 St[illegible] St., Albany.
Time: Third Wednesday in October, November, Marc[illegible] April, May and June.

Fort Worth Eye, Ear, Nose and Throat Soci[illegible]

President: Dr. Rex Howard, 602 W. 10th St., Fo[illegible] Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Ar[illegible] Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:[illegible] p. m., first Friday of each month except July a[illegible] August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Av[illegible] Houston, Texas.
Secretary: Dr. John T. Stough, 803 Medical Ar[illegible] Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medica[illegible] Society Rooms. Time: 8 p. m., second Thursday o[illegible] each month from September to June.

Indianapolis Ophthalmoolgical and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m. second Thursday of each month from November t[illegible] May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansa[illegible] City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansa[illegible] City, Mo.
Time: Third Thursday of each month from October t[illegible] June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Francis Carl Hertzog, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Robert G. Thornburgh, 117 E. 8th St., Long Beach, Calif.
Place: Seaside Hospital. Time: Last Wednesday o[illegible] each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.
Secretary-Treasurer: Dr. K. C. Brandenburg, 110 Pin[illegible] Ave., Long Beach 2, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time 6:30 p. m., fourth Mon[illegible] day of each month from September to May, inclusive

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.
Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montreal Ophthalmological Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6.30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville, Tenn.
Place: James Robertson Hotel. Time 6:30 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Rudolf Aebli, 30 E. 40th St., New York.
Secretary: Dr. Truman L. Boyes, 654 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Maurice L. Wieselthier, 1322 Union St., Brooklyn.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York 28.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. A. A. Steinberg, 1502 Farnam St., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha 2.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Clarence F. Bernatz, Park Bldg., Pittsburgh.
Secretary: Dr. Robert J. Billings, Park Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July. August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Isaac B. High, 326 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Eye, Ear, Nose and Throat Society

President: Dr. Luther C. Brawner, Professional Bldg., Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. Vincent Jones, 634 N. Grand Blvd., St. Louis.
Secretary: Dr. T. E. Sanders, 508 N. Grand Blvd., St. Louis 3.
Place: Oscar Johnson Institute. Time: Fourth Friday of each month from October to April, inclusive, except December, at 8:00 p. m.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery B
Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical
Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30
first Monday of every month except July, A
and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. R
side Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey, 421 W. R
side Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fou
Tuesday of each month except June, July and Au

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee
Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713
Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of e
month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. L. C. Ravin, 316 Michigan St., Tole
Ohio.
Secretary: Dr. W. W. Randolph, 1838 Parkwood A
Toledo, Ohio.
Place: Toledo Club. Time: Each month except J
July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts B
Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts B
Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. T
First Monday of each month, November to A

Washington, D. C., Ophthalmological Socie

President: Dr. Harold M. Downey, 1740 M St. N.
Washington, D. C.
Secretary-Treasurer: Dr. Richard W. Wilkinson,
L St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia B
1718 M St. N. W., Washington, D. C. Time: 7
p. m., first Monday in November, January, M
and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Fran
St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday
each month from October to May.